130 mm x 180 mm

Front

Censipar

(Cinacalcet)

Tablet

سینسی پار

COMPOSITION:
Censipar Tablet 30 mg:
Each film coated tablet contains:
Cinacalcet as hydrochloride ..... 30 mg.

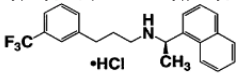
Product Specs.: Innovator

Censipar Tablet 60 mg:

Each film coated tablet contains:
Cinacalcet as hydrochloride ..... 60 mg.

Product Specs.: Innovator

DESCRIPTION:
Cinacalcet is a calcimimetic agent that increases the sensitivity of the calcium-sensing receptor to activation by extracellular calcium. Cinacalcet tablets contain the hydrochloride salt of cinacalcet. Its empirical formula is $C_{22}H_{22}F_3N$•HCl with a molecular weight of 393.9 g/mol (hydrochloride salt) and 357.4 g/mol (free base). It has one chiral center having an R-absolute configuration. The R-enantiomer is the more potent enantiomer and has been shown to be responsible for pharmacodynamic activity. The hydrochloride salt of cinacalcet is a white to off-white, crystalline solid that is soluble in methanol or 95% ethanol and slightly soluble in water. The hydrochloride salt of cinacalcet is described chemically as N-[1-(R)-(-)-(1-naphthyl)ethyl]-3-[3(trifluoromethyl)phenyl]-1-aminopropane hydrochloride and has the following structural formula:



CLINICAL PHARMACOLOGY:
Mechanism of Action:
Secondary HPT in patients with CKD is a progressive disease, associated with increases in PTH levels and derangements in calcium and phosphorus metabolism. Increased PTH stimulates osteoclastic activity resulting in cortical bone resorption and marrow fibrosis. The goals of treatment of secondary HPT are to lower the levels of PTH, calcium, and phosphorus in the blood in order to prevent progressive bone disease and the systemic consequences of disordered mineral metabolism. Reductions in PTH are associated with a decrease in bone turnover and bone fibrosis in patients with CKD on dialysis and uncontrolled secondary HPT. The calcium-sensing receptor on the surface of the chief cell of the parathyroid gland is the principal regulator of PTH synthesis and secretion. Cinacalcet directly lowers PTH levels by increasing the sensitivity of the calcium-sensing receptor to extracellular calcium. The reduction in PTH is associated with a concomitant decrease in serum calcium levels.
Pharmacodynamics:
Reduction in iPTH levels correlated with the plasma cinacalcet concentrations in patients with CKD. The nadir in iPTH level occurs approximately 2 to 6 hours post dose, corresponding with the maximum plasma concentration (C_{max}) of cinacalcet. After steady-state cinacalcet concentrations are reached (which occurs within 7 days of dose change), serum calcium concentrations remain constant over the dosing interval in
patients with CKD.
Pharmacokinetics:
Absorption and distribution: After oral administration of cinacalcet, C_{max} is achieved in approximately 2 to 6 hours. Cinacalcet C_{max} and AUC(0-inf) were increased by 82% and 68%, respectively, following administration with a high-fat meal compared with fasting in healthy volunteers. The Cmax and AUC(0-inf) of cinacalcet were increased by 65% and 50%, respectively, when cinacalcet was administered with a low-fat meal compared with fasting. After absorption, cinacalcet concentrations decline in a biphasic fashion with a terminal half-life of 30 to 40 hours. Steady-state drug levels are achieved within 7 days, and the mean accumulation ratio is approximately 2 with once daily oral administration. The median accumulation ratio is approximately 2 to 5 with twice daily oral administration. The AUC and C_{max} (0-inf) of cinacalcet increase proportionally over the dose range of 30 to 180 mg once daily. The pharmacokinetic profile of cinacalcet does not change over time with once daily dosing of 30 to 180 mg. The volume of distribution is approximately 1000 L, indicating extensive distribution. Cinacalcet is approximately 93% to 97% bound to plasma protein(s). The ratio of blood cinacalcet concentration to plasma cinacalcet concentration is 0.80 at a blood cinacalcet concentration of 10 ng/mL.
Metabolism and excretion: Cinacalcet is metabolized by multiple enzymes, primarily CYP3A4, CYP2D6, and CYP1A2. After administration of a 75 mg radiolabeled dose to healthy volunteers, cinacalcet was metabolized via: 1) oxidative N-dealkylation to hydrocinnamic acid and hydroxy-hydrocinnamic acid, which are further metabolized via ß-oxidation and glycine conjugation; the oxidative N-dealkylation process also generates metabolites that contain the naphthalene ring; and 2) oxidation of the aphthalene ring on the parent drug forming dihydrodiols, which are further conjugated with glucuronic acid. The plasma concentrations of the major circulating metabolites, including the cinnamic acid derivatives and glucuronidated dihydrodiols, markedly exceed the parent drug concentrations. The hydrocinnamic acid metabolite and glucuronide conjugates have minimal or no calcimimetic activity. Renal excretion of metabolites was the primary route of elimination of radioactivity. Approximately 80% of the dose was recovered in the urine and 15% in the feces.
Special Populations:
Hepatic impairment: Cinacalcet exposure (AUC(0-inf)) was comparable between healthy volunteers and patients with mild hepatic impairment. However, in patients with moderate and severe hepatic impairment (as indicated by the Child-Pugh method), cinacalcet exposures (AUC(0-inf)) were 2.4 and 4.2-fold higher, respectively, than that in healthy volunteers. The mean half-life of cinacalcet increased from 49 hours in healthy volunteers to 65 hours and 84 hours in patients with moderate and severe hepatic impairment, respectively. Protein binding of cinacalcet is not affected by impaired hepatic function.
Renal impairment: The pharmacokinetic profile of a 75 mg Cinacalcet single dose in patients with mild, moderate, and severe renal impairment, and those on hemodialysis or peritoneal dialysis is comparable with that in healthy volunteers.
Geriatric patients: The pharmacokinetic profile of cinacalcet in geriatric patients age 65 years is similar to that for patients who are < 65 years of age.
Pediatric patients: The pharmacokinetics of cinacalcet has not been studied in patients < 18 years of age.

DRUG INTERACTIONS:
Strong CYP3A4 inhibitors: Cinacalcet is partially metabolized by CYP3A4. Dose adjustment of Cinacalcet may be required if a patient initiates or discontinues therapy with a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole). The iPTH and serum calcium concentrations should be closely monitored in these patients.
CYP2D6 substrates: Cinacalcet is a strong inhibitor of CYP2D6. Dose adjustments may be required for concomitant medications that are predominantly metabolized by CYP2D6 (e.g., desipramine, metoprolol, and carvedilol) and particularly those with a narrow therapeutic index (e.g., flecainide and most tricyclic antidepressants).

INDICATION & USAGE:
Secondary hyperparathyroidism: Cinacalcet is indicated for the treatment of secondary hyperparathyroidism (HPT) in patients with chronic kidney disease (CKD) on dialysis.
Parathyroid carcinoma: Cinacalcet is indicated for the treatment of hypercalcemia in patients with Parathyroid Carcinoma.
Primary hyperparathyroidism: Cinacalcet is indicated for the treatment of severe hypercalcemia in patients with primary HPT who are unable to undergo parathyroidectomy.

DOSAGE AND ADMINISTRATION:
Cinacalcet tablets should be taken whole and should not be divided. Cinacalcet should be taken with food or shortly after a meal. Dosage must be individualized.

Back

Secondary hyperparathyroidism in patients with chronic kidney disease on dialysis: The recommended starting oral dose of Cinacalcet is 30 mg once daily. Serum calcium and serum phosphorus should be measured within 1 week and intact parathyroid hormone (iPTH) should be measured 1 to 4 weeks after initiation or dose adjustment of Cinacalcet. Cinacalcet should be titrated no more frequently than every 2 to 4 weeks through sequential doses of 30, 60, 90, 120, and 180 mg once daily to target iPTH levels of 150 to 300 pg/mL. Serum iPTH levels should be assessed no earlier than 12 hours after dosing with Cinacalcet. Cinacalcet can be used alone or in combination with vitamin D sterols and/or phosphate binders. During dose titration, serum calcium levels should be monitored frequently and if levels decrease below the normal range, appropriate steps should be taken to increase serum calcium levels, such as by providing supplemental calcium, initiating or increasing the dose of calcium-based phosphate binder, initiating or increasing the dose of vitamin D sterols, or temporarily withholding treatment with Cinacalcet.
Parathyroid carcinoma and primary hyperparathyroidism: The recommended starting oral dose of Cinacalcet is 30 mg twice daily. The dose of Cinacalcet should be titrated every 2 to 4 weeks through sequential doses of 30 mg twice daily, 60 mg twice daily, and 90 mg twice daily, and 90 mg 3 or 4 times daily as necessary to normalize serum calcium levels.

CONTRAINDICATIONS:
Hypocalcemia:
Cinacalcet treatment should not be initiated if serum calcium is less than the lower limit of the normal range.
- History of serious hypersensitivity reaction to any ingredient.

WARNINGS AND PRECAUTIONS:
Hypocalcemia: Cinacalcet lowers serum calcium and, therefore, patients should be carefully monitored for the occurrence of hypocalcemia. Potential manifestations of hypocalcemia include paresthesia's, myalgias, muscle cramping, tetany, and convulsions. Serum calcium should be measured within 1 week after initiation or dose adjustment of Cinacalcet. Once the maintenance dose has been established, serum calcium should be measured approximately monthly. If serum calcium falls below 8.4 mg/dL but remains above 7.5 mg/dL, or if symptoms of hypocalcemia occur, calcium-containing phosphate binders and/or vitamin D sterols can be used to raise serum calcium. If serum calcium falls below 7.5 mg/dL, or if symptoms of hypocalcemia persist and the dose of vitamin D cannot be increased, withhold administration of Cinacalcet until serum calcium levels reach 8.0 mg/dL and/or symptoms of hypocalcemia have resolved. Treatment should be reinitiated using the next lowest dose of Cinacalcet. In patients with secondary HPT and CKD not on dialysis, the long-term safety and efficacy of Cinacalcet have not been established. Clinical studies indicate that Cinacalcet-treated patients with CKD not on dialysis have an increased risk for hypocalcemia compared with Cinacalcet-treated patients with CKD on dialysis, which may be due to lower baseline calcium levels.
Seizures: Cases of seizures (primarily generalized or tonic-clonic) have been reported. Therefore, serum calcium levels should be closely monitored in patients receiving Cinacalcet, particularly in patients with a history of a seizure disorder.
Hypotension and/or worsening heart failure: Isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia have been reported in patients with impaired cardiac function which may be mediated by reductions in serum calcium levels.
Adynamic bone disease: Adynamic bone disease may develop if iPTH levels are suppressed below 100 pg/mL. If iPTH levels decrease below 150 pg/mL in patients treated with Cinacalcet, the dose of Cinacalcet and/or vitamin D sterols should be reduced or therapy discontinued.
Hepatic impairment: Cinacalcet exposure, as defined by the Area Under the Curve (AUC0-inf), is increased by 2.4 and 4.2-fold in patients with moderate and severe hepatic impairment, respectively. These patients should be monitored throughout treatment with Cinacalcet.
Laboratory tests:
Secondary hyperparathyroidism in patients with chronic kidney disease on dialysis: Serum calcium and serum phosphorus should be measured within 1 week and iPTH should be measured 1 to 4 weeks after initiation or dose adjustment of Cinacalcet. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and iPTH every 1 to 3 months. In patients with end-stage renal disease, testosterone levels are often below the normal range.
Patients with parathyroid carcinoma or primary hyperparathyroidism: Serum calcium should be measured within 1 week after initiation or dose adjustment of Cinacalcet. Once maintenance dose levels have been established, serum calcium should be measured every 2 months.
Use in Specific Population:
Pregnancy:
Category C:
There are no adequate and well-controlled studies of Cinacalcet in pregnant women. Cinacalcet should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Nursing mothers: There is a potential for clinically significant adverse reactions in infants who ingest Cinacalcet, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the lactating woman.
Pediatric use: The safety and efficacy of Cinacalcet in pediatric patients have not been established.
Geriatric use: No differences in the safety and efficacy of Cinacalcet were observed in patients greater or less than 65 years of age. No dosage adjustment is required for geriatric patients.

ADVERSE REACTIONS:
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice.
The following important adverse reactions are described below and elsewhere in the labeling: The most frequently reported adverse reactions were nausea, vomiting, and diarrhea. Other reported adverse events include rash, hypersensitivity reactions (including angioedema and urticaria), myalgia, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmias, seizures, dizziness, asthenia, anorexia and chest pain.

OVER DOSAGE:
Doses titrated up to 300 mg once daily have been safely administered to patients on dialysis. Overdosage of Cinacalcet may lead to hypocalcemia. In the event of overdosage, patients should be monitored for signs and symptoms of hypocalcemia and appropriate measures taken to correct serum calcium levels. Since Cinacalcet is highly protein bound, hemodialysis is not an effective treatment for overdosage of Cinacalcet.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Censipar Tablet 30 mg	:	Pack of 1 x 10 tablets.
Censipar Tablet 60 mg	:	Pack of 1 x 10 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT:

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