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Revised: Aug 2022

ATC code
H05BX01

- DRUG FOR TREATMENT OF SECONDARY HYPERPARATHYROIDISM –

(CALCIUM RECEPTOR AGONIST)

Prescription drug: Caution – Use only as directed by a physician.

REGPARA® TABLETS 25mg

< Cinacalcet Hydrochloride Tablets >

Storage
Store below 30°C. **Protect from light.**

Expiration date
Specified on the outer package.

	Regpara Tablets 25 mg
Approval No.	21900AMX01750
Date of listing in the NHI reimbursement price	December 2007
Date of initial marketing in Japan	January 2008
International birth date	March 2004

CONTRAINDICATIONS (Regpara is contraindicated in the following patients.)

Patients with a history of hypersensitivity to any of the ingredients in Regpara.

DESCRIPTION

Brand name	Regpara Tablets 25 mg
Active ingredients (per tablet)	Cinacalcet hydrochloride 27.55 mg (including 25 mg of cinacalcet)
Additives	Partly pregelatinized starch, microcrystalline cellulose, povidone, crospovidone, light anhydrous silicic acid, talc, magnesium stearate, lactose hydrate, hypromellose, titanium oxide, triacetin, macrogol 400, yellow ferric oxide, blue No. 2 aluminium lake

Colour	Light-green to light-yellowish green
Dosage form	Film-coated tablets
Appearance	Face:  Rear:  Side: 
Diameter	8 mm
Thickness	4 mm
Weight	ca. 207 mg
Identification code	KR02

INDICATIONS
Secondary hyperparathyroidism in patients undergoing maintenance dialysis

DOSAGE AND ADMINISTRATION
The starting dosage for adults is 25 mg of cinacalcet once daily, to be orally administered.
With careful management of the patient's serum parathyroid hormone (PTH) and calcium levels, the dose may then be adjusted within a range of 25-75 mg once daily. If no improvement found in PTH, the dose may be increased up to 100 mg once daily. If dose increase is required, dose should be increased by 25 mg at a time, at intervals of at least 3 weeks.

<Precautions related to Dosage and Administration>
1. Regpara has an effect of decreasing calcium in blood. Therefore, it should be confirmed that the patient's serum calcium level is not low (9.0 mg/dL (2.3mmol/L) or more) prior to administration.

2. The serum calcium level should be determined once a week at the start of administration and during the dose adjustment period, and at least once every two weeks during the maintenance period. If serum calcium level decreases to 8.4 mg/dL (2.1mmol/L) or less, the following measures should be taken.

<table>
<tr><td rowspan="2">Serum calcium level</td><td colspan="4">Measures to be taken</td></tr>
<tr><td colspan="2">Actions
Administration of Regpara</td><td>Examinations</td><td>Dose increase/ Restart of treatment</td></tr>
<tr><td colspan="2">8.4 mg/dL (2.1mmol/L) or less</td><td>In principle, the dose should not be increased (should be decreased as needed.)</td><td rowspan="2">Administration of calcium or vitamin D preparations should be considered.</td><td rowspan="2">The serum calcium level should be determined at least once a week.

It is recommended to perform electrocardiography.</td><td>If the dose is increased, the serum calcium level should be confirmed to have recovered to 8.4 mg/dL (2.1mmol/L) or more prior to dose increase.</td></tr>
<tr><td></td><td>7.5mg/dL (1.9mmol/L) or less</td><td>The drug should be withdrawn immediately.</td><td>If the treatment is restarted, the serum calcium level should be confirmed to have recovered to 8.4 mg/dL (2.1mmol/L) or more prior to restart, and then the resumption dose should be set at the pre-withdrawal level or less.</td></tr>
</table>

The serum calcium level should be determined before administration of Regpara so that the effect and safety of the drug may be properly evaluated. Furthermore, it is recommended that corrected serum calcium values[Note)] should be used as a guide in patients with hypoalbuminemia (serum albumin: <4.0 g/dL).

3. The serum PTH level should be periodically determined so that it may be maintained at the target level for management. It is recommended that the serum PTH level should be determined twice a month at the start of administration and during the dose adjustment period (about 3 months after the start of administration), and at least once a month after the serum PTH level is confirmed to be almost stable. The serum PTH level should be determined before administration of Regpara so that the effect and safety of the drug may be properly evaluated.

Note) Corrected serum calcium is calculated as follows:
Corrected serum calcium (mg/dL) = Serum calcium (mg/dL) − Serum albumin (g/dL) + 4.0

PRECAUTIONS

1. Precautions Concerning Patients with Specific Backgrounds

Patients with Complication or History of Diseases, etc.

(1) Patients with hypocalcemia [Hypocalcemia may be aggravated.] (See “Precautions related to dosage and administration”, “Important Precautions” and “Clinically Significant Adverse Reactions”.)

(2) Patients with seizure or a history of seizure [It has been reported in a clinical study outside Japan that seizure occurred in patients with a history of seizure.]

(3) Patients with hepatic impairment [The exposure amount will be increased since cinacalcet is metabolized in the liver.] (See “Patients with Specific Backgrounds”)

(4) Patients with active or a history of gastrointestinal hemorrhage, gastrointestinal ulcer [Symptoms may worsen or recur.] (See “Clinically Significant Adverse Reactions”)

2. Important Precautions

(1) During treatment with Regpara, sufficient caution should be exercised to avoid hypocalcemia by periodical measurement of the serum calcium level. If hypocalcemia occurs or may occur, administration of calcium or vitamin D preparations should be considered, as well as reducing the dose of Regpara. If administration of calcium or vitamin D preparations is discontinued during treatment with Regpara, caution should be exercised for possible occurrence of hypocalcemia. (See “Precautions related to dosage and administration”, “Precautions Concerning Patients with Specific Backgrounds” and “Clinically Significant Adverse Reactions”).

(2) At the start of administration and during the dose adjustment period, the patient’s symptoms should be frequently monitored and caution should be exercised for possible occurrence of adverse reactions.

3. Drug interactions

Precautions for co-administration (Regpara should be administered with care when co-administered with the following drugs.)

Drugs	Signs, Symptoms and Treatment	Mechanism and Risk Factors
Azole antifungals Itraconazole, etc. Macrolide antibiotics Erythromycin, Clarithromycin, etc. Amiodarone hydrochloride Grapefruit juice	The blood concentration of cinacalcet may increase and the effect of the drug may enhance.	Cinacalcet metabolism mainly involves CYP3A4. Therefore, the co-administration of CYP3A4 inhibitors, listed in the left column, with cinacalcet have a potency to inhibit the cinacalcet metabolism and lead to an increase of plasma cinacalcet concentration. The AUC of cinacalcet increased about two-fold when cinacalcet was co-administered with ketoconazole[1)].
Tricyclic antidepressant Amitriptyline hydrochloride, Imipramine hydrochloride, etc. Butyrophenone antipsychotics Haloperidol, etc. Flecainide acetate Vinblastine sulfate	The blood concentration of these drugs may increase.	Cinacalcet is an inhibitor of CYP2D6. Therefore, the co-administration of cinacalcet with CYP2D6 substrates listed in the left column has a potency to inhibit the metabolism of those CYP2D6 substrates and lead to an increase of their blood concentrations. The AUC of dextromethorphan increased about eleven-fold when dextromethorphan hydrobromide was co-administered with cinacalcet[2)].
Calcitonin Bisphosphonates, inhibitors of bone absorption Pamidronate sodium hydrate Alendronate sodium hydrate, Incadronate disodium, etc. Corticosteroids Cortisol, Prednisolone, Dexamethasone, etc.	The serum calcium level may decrease.	The blood calcium-decreasing effect of cinacalcet may be strengthened.
Digitoxin, diazepam, etc.	The blood concentration of cinacalcet may be affected.	The degree of plasma protein-binding of cinacalcet is high.

4. Adverse Reactions

The following adverse reactions may occur. Patients must therefore be carefully monitored. If any abnormalities are observed, appropriate measures should be taken, including discontinuing administration.

(1) Clinically Significant Adverse Reactions

1) **Hypocalcemia/decreased serum calcium** (13.7%): If symptoms considered attributable to hypocalcemia (prolonged QT interval, numbness, cramping, feeling unwell, arrhythmia, decreased blood pressure, seizure, etc.) occur, the serum calcium level should be confirmed, and administration of calcium or vitamin D preparations considered. (See “Precautions related to dosage and administration”, “Important Precautions”, “Precautions Concerning Patients with Specific Backgrounds”, “Overdosage” and below point 2.)

2) **Prolonged QT interval** (5.3%): (See above point 1)

3) **Gastrointestinal hemorrhage, gastrointestinal ulcer (incidence unknown):** (See “Precautions Concerning Patients with Specific Backgrounds”)

4) **Decreased level of consciousness** (0.2%)**, temporary loss of consciousness** (0.2%)

5) **Sudden death** (0.3%): Unexplained sudden death has been reported in patients treated with Regpara.

(2) Other adverse reactions

	≥ 5%	1% to < 5%	< 1%	Incidence unknown
Gastrointestinal	Nausea/ vomiting (25.1%), gastric discomfort (17.1%), anorexia, abdominal distension	Upper abdominal pain, diarrhea, constipation, gastroduodenitis, dyspepsia, abdominal discomfort, gastrointestinal disorder, reflux esophagitis, abdominal pain	Gastric ulcer, stomatitis, epigastric discomfort, fecal occult blood, gastroenteritis, hemorrhoids, hiatal hernia	
Cardiovascular		Increased blood pressure, arrhythmia	Decreased blood pressure, myocardial infarction, ventricular extrasystoles, atrial fibrillation, palpitations, myocardial ischemia, supraventricular extrasystoles, tachycardia	

Psycho-Neurological		Headache, numbness, dizziness, paraesthesia, insomnia		
Musculoskeletal		Muscle spasm, pain in extremities, arthralgia	Myalgia, stiffness	
Metabolic			Increased CK (CPK), increased LDH, increased blood sugar, dehydration, hyperlipidemia, increased total cholesterol	
Sensory		Taste abnormality		
Hepatic		Increased Al-P	Increased AST / ALT	Increased bilirubin, increased gamma-GTP
Ophthalmic			Conjunctival hemorrhage, dry eye	
Skin		Pruritus	Rash, alopecia, subcutaneous hemorrhage	
Endocrine			Goitre	
Hematologic		Anemia	Decreased platelets	
Others		Malaise, edema	Feeling bad, weakness, chest discomfort, thirst, weight decreased, shunt occlusion, chest pain, pyrexia, erectile dysfunction	

5. Use in the Elderly

If any adverse reactions are observed, appropriate measures such as reducing the dose should be taken. Patients aged 65 years or older have been reported to show higher incidences of adverse reactions (prolonged QT interval in particular) than those younger than 65 years.

6. Use during Pregnancy or Lactation

(1) It is recommended not to use Regpara in pregnant women or in women who may possibly be pregnant. The safety of Regpara during pregnancy has not been established. Hypocalcemia, suppressed weight gain and decreased food consumption in dams, as well as decreased weight in fetuses, were observed in

animal studies (using rats and rabbits). Furthermore, cinacalcet was reported to be transferred through the placenta in animal studies (using rats and rabbits).

(2) It is not known whether cinacalcet is excreted in human milk. Cinacalcet is excreted in the milk of lactating rats with a high milk to plasma ratio. A transient suppression of weight gain was also observed in rats newborns. Following careful benefit/risk assessment, a decision should be made to discontinue either breast-feeding or treatment with cinacalcet.

7. Pediatric Use

Clinical trials on the efficacy and safety in children have not been conducted.

8. Overdosage

Symptoms: Overdosage of Regpara is considered to cause hypocalcemia.
Actions: The patient should be monitored for any signs or symptoms of hypocalcemia. If hypocalcemia occurs or may occur, drip infusion of calcium preparations should be taken into consideration. Regpara is not eliminated by hemodialysis (See “Clinically Significant Adverse Reactions”).

9. Precautions Concerning Use

Precautions concerning the dispensing of the drug

In the case of a press-through package (PTP), the patient should be instructed to remove the drug from the package prior to use. If a PTP sheet is mistakenly swallowed, the sharp corners of the sheet may puncture the esophageal mucosa and thereby cause perforation, leading to serious complications such as mediastinitis.

10. Other Precautions

Information Based on Clinical Use

(1) In a clinical study outside Japan in which cinacalcet hydrochloride was used in patients with chronic renal failure accompanied by secondary hyperparathyroidism who had not yet started dialysis, it has been reported that the serum calcium level tended to be lower than the lower limit of the normal range (8.4 mg/dL (2.1mmol/L)) compared to that in patients receiving dialysis[3)]. Use of the drug in patients with chronic renal failure accompanied by secondary hyperparathyroidism who have not yet been on dialysis has not been approved.

(2) It has been reported abroad that adynamic bone disease occurred due to an excessive decrease in PTH following administration of cinacalcet.

(3) It has been reported aboard that hungry bone syndrome accompanied by hypocalcemia and hypophosphatemia occurred due to a rapid decrease in PTH following administration of cinacalcet.

PHARMACOKINETICS

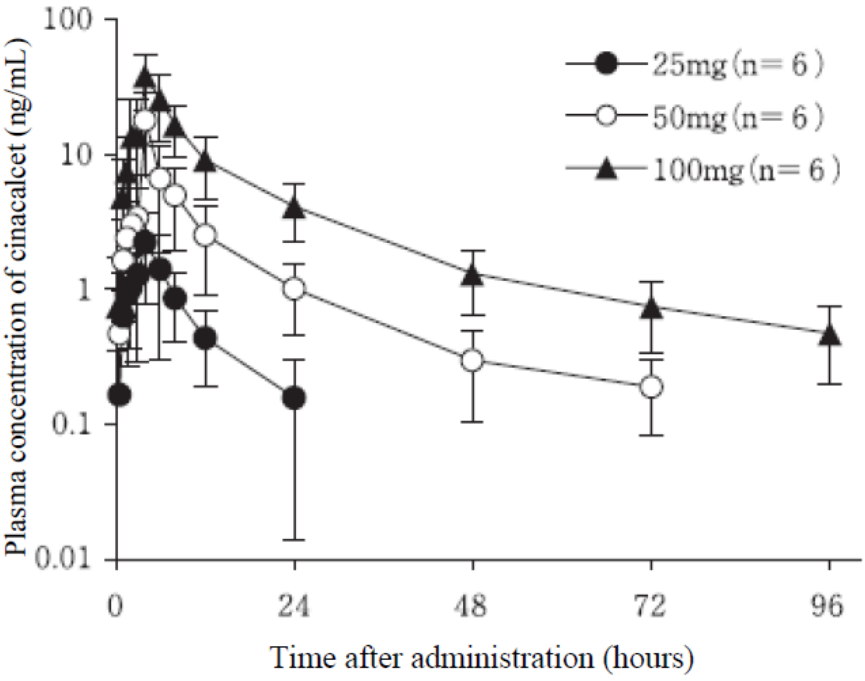
1. Blood level

a. Single administration

i. Healthy adult subjects

Single oral administration of cinacalcet at doses of 25, 50, and 100 mg during fasting condition to healthy adult subjects was conducted to evaluate the pharmacokinetics of cinacalcet. The plasma concentration of cinacalcet increased dose dependently, and showed biphasic elimination. The pharmacokinetic parameters are summarized below[4)].

Plasma concentration profiles of cinacalcet after single oral administration of cinacalcet hydrochloride to healthy adult subjects (Mean±S.D.)



Pharmacokinetic parameters of cinacalcet after single administration of cinacalcet hydrochloride to healthy adult subjects

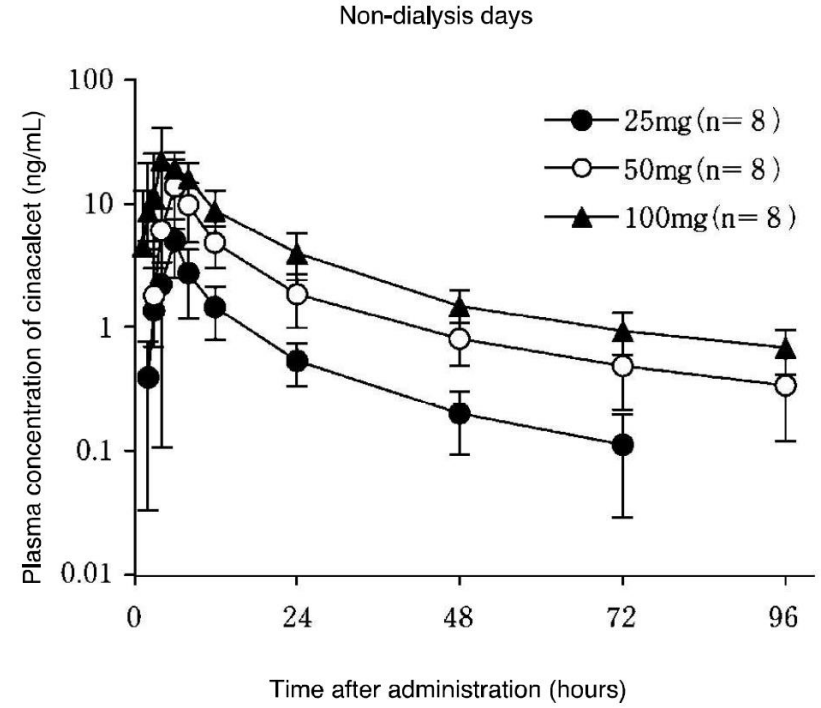
Dose (mg)	Pharmacokinetic parameters	
25	C_{max}(ng/mL)	2.63±1.23
	t_{max}(h)	3.9±1.4
	AUC(ng•h/mL)	18.5±10.5
	$t_{1/2}$(h)	7.70±3.54
50	C_{max}(ng/mL)	17.73±10.89
	t_{max}(h)	4.0±0.0
	AUC(ng•h/mL)	117.7±65.7
	$t_{1/2}$(h)	24.81±9.41
100	C_{max}(ng/mL)	41.88±12.19
	t_{max}(h)	4.0±1.3
	AUC(ng•h/mL)	409.8±160.3
	$t_{1/2}$(h)	32.22±5.63

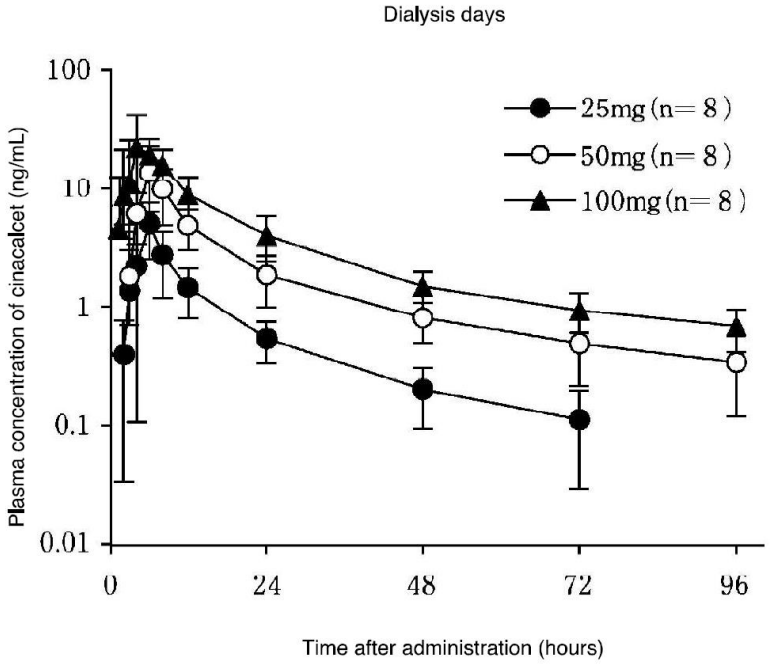
Mean±S.D., n=6

ii. Hemodialysis patients

Single oral administration of cinacalcet at doses of 25, 50, and 100 mg during fasting condition to hemodialysis patients (Japanese) was conducted to evaluate the pharmacokinetics of cinacalcet. The plasma concentration of cinacalcet increased dose dependently both on the non-dialysis day and dialysis day, and showed biphasic elimination. The pharmacokinetic parameters are summarized below, and no effect of hemodialysis was observed[5].

Plasma concentration profiles of cinacalcet after single administration of cinacalcet hydrochloride to hemodialysis patients (Mean±S.D.)





Pharmacokinetic parameters of cinacalcet after single oral administration of cinacalcet to hemodialysis patients with secondary hyperparathyroidism

Dose (mg)	Pharmacokinetic parameters	Non-dialysis days	Dialysis days
25	C_{max} (ng/mL)	5.16 ± 2.34	9.92 ± 6.64
	t_{max} (hr)	5.6 ± 1.1	4.8 ± 1.4
	AUC (ng·hr/mL)	57.6 ± 25.1	85.4 ± 26.0
	$t_{1/2}$ (hr)	28.45 ± 14.24	32.94 ± 14.52
50	C_{max} (ng/mL)	17.89 ± 10.00	20.71 ±13.71
	t_{max} (hr)	6.0 ± 1.1	4.6 ± 1.6
	AUC (ng·hr/mL)	207.1 ± 91.8	218.6 ± 99.6
	$t_{1/2}$ (hr)	38.58 ± 20.19	33.96 ± 10.23
100	C_{max} (ng/mL)	26.92 ± 15.80	36.70 ± 26.09
	t_{max} (hr)	4.8 ± 1.8	4.4 ± 1.8
	AUC (ng·hr/mL)	383.3 ± 126.5	408.4 ± 125.8
	$t_{1/2}$ (hr)	38.47 ± 8.62	40.12 ± 7.50

Mean±Standard Deviation, n=8 for C_{max}, t_{max}, n=7 for others

b. Plasma concentration profiles and multiple oral administration

In healthy adult subjects given multiple oral doses of cinacalcet at 50 mg for 7 days, trough plasma concentration of cinacalcet reached steady state within 7 days.

The plasma trough concentration profiles of cinacalcet after multiple oral administration to hemodialysis patients (Japanese) were examined in a period of up to 53 weeks. No tendency of increasing or decreasing over time was observed in the trough concentration, and the plasma concentration was confirmed to have reached a steady state following repeated-dose administration.

2. Absorption

a. Bioavailability

The bioavailability (mean value) of cinacalcet (25 to 100 mg) was 5.1 to 28.4% (Japan) and 7.9 to 24.4% (outside Japan)[6].

b. Food-effect

Single oral administration at a dose of 50 mg to healthy volunteers (Japanese) was conducted to evaluate the food-effect on the pharmacokinetics of cinacalcet. The pharmacokinetic parameters of non-fasting condition were almost similar to those of fasting condition, suggesting that the effect of food on the pharmacokinetics of cinacalcet was small[7].

3. Distribution

In vitro protein-binding of cinacalcet (25 - 100 ng/mL) in human plasma was 96.67 - 97.67% in males and 94.33 - 97.67% in females, respectively, and no difference between males and females was observed[8]. The protein binding of cinacalcet was also analyzed in special population clinical studies, such as hepatic and renal impairment population (non-Japanese). The protein binding was found to be similar among normal, hepatic impairment and renal impairment population, which was 94.7 - 97.1% for normal and hepatic

impairment population, and 92.7 - 95.1% for normal and renal impairment population, respectively[9,10]. Cinacalcet was considered to be bound to albumin[8] and shown to have a high affinity to the site II[8,11]. [See “Precautions for co-administration”].

4. Metabolism

Single oral administration of ^{14}C-labelled cinacalcet at a dose of 75 mg to non-Japanese healthy adult subjects healthy adult subjects was conducted to evaluate the metabolism of cinacalcet. Cinacalcet was extensively metabolized via N-dealkylation and oxidation of naphthalene ring[12].

5. Excretion

The urinary excretion of unchanged drug after single oral administration to healthy volunteers (Japanese) was very low, and multiple administration of cinacalcet did not influence to the excretion of unchanged drug[13]. Following single-dose oral administration of 75 mg of ^{14}C-labelled cinacalcet to non-Japanese healthy adult subjects, cinacalcet was confirmed to be excreted mainly in urine as metabolities[12].

6. Patients with Specific Backgrounds

i. Patients with hepatic impairment

When the pharmacokinetics of a single oral administration of 50 mg of cinacalcet was examined in healthy subjects and patients with hepatic impairment under fasting condition, AUC increased 2.4-fold and 4.2-fold, respectively, in patients with moderate and advanced hepatic impairment by the Child-Pugh classification, compared to subjects with normal liver function. The AUC in patients with mild hepatic impairment by the Child-Pugh classification was similar to subjects with normal hepatic function[14]. [See “Patients with Complication or History of Diseases, etc.**”**]

7. Drug interactions

- No changes were observed in the pharmacokinetics of cinacalcet in combination with a drug which changes gastric pH (calcium carbonate) or a phosphorus adsorbent (sevelamer hydrochloride)[16,17] (data from non-Japanese).
- Cinacalcet has no effect on the pharmacokinetics of *R* and *S*-warfarin and pharmacodynamics of warfarin (i.e. prothrombin time and the activity of clotting factor VII)[15].

CLINICAL STUDIES

Clinical Studies for Efficacy and Safety

1. Phase III study in Japan (hemodialysis)

Cinacalcet or placebo was orally administered to 143 patients with secondary hyperparathyroidism on hemodialysis (cinacalcet-treated group: 72, placebo-treated group: 71) for 14 weeks with an initial dose of 25 mg once daily, which was titrated up to 100 mg. As a result, the rate of patients in whom serum intact PTH concentrations reached the target level (250 pg/mL or less) was shown to be 51.4% in the cinacalcet-treated group, which was significantly higher than 2.8% in the placebo-treated group (χ^2 = 42.521, $p<0.001$)[18].

The frequency of adverse reactions was 73.6% (53/72 cases). The main adverse reactions were nausea 33.3% (24/72), stomach discomfort 22.2% (16/72), vomiting 19.4% (14/72), malaise 9.7% (7/72) and dyspepsia 8.3% (6/72).

2. Phase II/III studies in Japan (hemodialysis)

The results of phase II/III studies in Japan of cinacalcet in 369 patients with secondary hyperparathyroidism undergoing hemodialysis were as follows[19-21].

- In 65 patients with secondary hyperparathyroidism undergoing hemodialysis, cinacalcet was started at the same dose as at the end of the dose-response study or lower. The dose was adjusted up to 100 mg and orally administered for 44 weeks. As a result, the rate of patients in whom serum intact PTH concentrations reached the target level (250 pg/mL or less) at the end of administration was 43.1%.
  The frequency of adverse reactions was 70.8% (46/65 cases). The main adverse reactions were nausea 18.5% (12/65), abdominal distension 16.9% (11/65), stomach discomfort 13.8% (9/65), anorexia 12.3% (8/65), and upper abdominal pain, gastrointestinal upset, vomiting and decreased appetite 7.7% each (5/65).
- Cinacalcet was orally administered to 105 patients with secondary hyperparathyroidism undergoing hemodialysis for 52 weeks with an initial dose of 12.5 mg[Note 1)] once daily, which was titrated up to 100 mg. As a result, the rate of patients in whom serum intact PTH concentrations reached the target level (250 pg/mL or less) at the end of administration was 43.8%.
- The frequency of adverse reactions was 84.8% (89/105 cases). The main adverse reactions were stomach discomfort 22.9% (24/105), hypocalcemia 21.9% (23/105), nausea 15.2% (16/105), electrocardiogram QT corrected interval prolonged 13.3% (14/105), and anorexia 11.4% (12/105).
- Cinacalcet was orally administered to 199 patients with secondary hyperparathyroidism undergoing hemodialysis for 52 weeks with an initial dose of 25 mg once daily, which was titrated up to 100 mg. As a result, the rate of patients in whom serum intact PTH concentrations reached the target level (250 pg/mL or less) at the end of administration was 57.8%.
- The frequency of adverse reactions was 72.5% (145/200 cases). The main adverse reactions were stomach discomfort 21.5% (43/200), nausea 14% (28/200), vomiting 9.5% (19/200), hypocalcemia 9.0% (18/200), and anorexia 7.5% (15/200).

Note1) The initial dose for secondary hyperparathyroidism in patients undergoing maintenance dialysis is 25 mg of cinacalcet once daily.

3. Phase III study in Japan (peritoneal dialysis)

Cinacalcet was orally administered to 29 patients with secondary hyperparathyroidism on peritoneal hemodialysis for 16 weeks with an initial dose of 25 mg once daily, which was titrated up to 100 mg. Consequently, the rate of patients in whom serum intact PTH concentrations reached the target level (250 pg/mL or less) was shown to be 24.1% when the administration was completed. Thus, it was confirmed that cinacalcet had an effect of decreasing the serum intact PTH concentration in patients with secondary hyperparathyroidism on peritoneal hemodialysis[22].

The frequency of adverse reactions was 75.9% (22/29 cases). The main adverse reactions were nausea 41.4% (12/29), vomiting, stomach discomfort 20.7% each (6/29), anorexia 17.2% (5/29), and abdominal distension, blood calcium decreased, blood pressure decrease and hypocalcemia 6.9% each (2/29).

PHARMACOLOGY

1. Actions/effects

(1) Inhibition of PTH Secretion *(in vitro)*

Cinacalcet was shown to inhibit PTH secretion from bovine parathyroid cells and human parathyroid cells dose-dependently[23,24].

(2) Suppression of proliferation of parathyroid cells

Following repeated-dose oral administration to partially nephrectomized rats, cinacalcet was shown to inhibit proliferation of parathyroid cells and thereby suppress progression of parathyroid hyperplasia[25].

(3) Decrease in serum PTH and calcium levels

Following single-dose oral administration to normal rats and partially nephrectomized rats, cinacalcet was shown to decrease the serum PTH and calcium levels dose-dependently[23].

(4) Suppression of bone disorder

In patients with secondary hyperparathyroidism, bone disorder develops due to increased serum PTH levels. Following repeated-dose oral administration to partially nephrectomized rats, cinacalcet was shown to suppress symptoms associated with bone disorder due to increased serum PTH, such as marrow fibrosis, cortical osteoporosis, and decreases in cortical bone density and bone strength.

2. Mechanism of Actions

Cinacalcet exerts its effects via calcium receptors on the surface of parathyroid cells. Calcium receptors regulate synthesis of PTH and proliferation of parathyroid cells, as well as secretion of PTH. Cinacalcet decreases the serum PTH level by acting on calcium receptors and mainly suppressing PTH secretion. Furthermore, in repeated-dose administration, its effect of suppressing proliferation of parathyroid cells is also considered to contribute to a decrease in serum PTH level[23-25].

PHYSIOCOCHEMISTRY

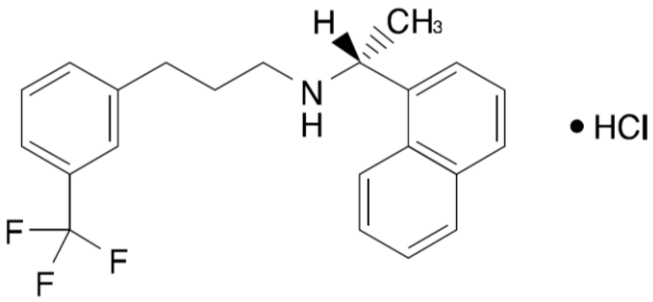
Nonproprietary name : Cinacalcet hydrochloride (JAN)

Chemical name : *N*-[(1*R*)-1-(Naphthalen-l-yl) ethyl]-3-[3-(trifluoromethyl) phenyl] propan-1-amine monohydrochloride

Molecular formula : $C_{22}H_{22}F_3N \cdot HCl$

Molecular weight : 393.87

Structural formula :



Description : Cinacalcet hydrochloride occurs as a white to slightly yellowish white, crystalline powder. It is freely soluble in *N,N*-dimethylformamide, methanol, and ethanol (99.5),

slightly soluble in water, and practically insoluble or insoluble in hexane.

Melting point : Approximately 181°C

PACKAGING

REGPARA Tablets 25 mg 100 tablets (PTP)

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