

Cinacalcet citrate

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Section – 1: Product and Company Identification
Product Name: Cinacalcet Hydrochloride Tablets

Common Name: Cinacalcet Hydrochloride

Chemical Name: N-[1-(R)-(-)-(1-naphthyl)ethyl]-3-[3-(trifluoromethyl)phenyl]-1-aminopropane

Synonyms: Sensipar, Mimpara, Parareg, AMG 073 and Cinacalcet HCl

CAS-No: 364782-34-3

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Section – 2: Hazard Identifications
Emergency Overview

The pharmacological and most common clinical effect of Cinacalcet HCl is to lower serum calcium and gastrointestinal effects (nausea and vomiting) respectively. These effects may potentially occur if exposures repeatedly exceed the Occupational Exposure Limit described below. Hypocalcemia is aggravated by exposure. Maybe harmful if swallowed.

2.1 - Classification of the drug substance or mixture (drug product in final form, not applicable)
REGULATION (EC) No 1272/2008

Serious Eye Damage / Eye Irritation	Category 1
Skin Sensitization	Sub-category 1B
Specific TOST - Repeated Exposure Oral	Category 2 eyes and cecum
Acute Aquatic Toxicity	Acute 1
Chronic Aquatic Toxicity	Chronic 1

Classification according to EU Directives 67/548/EEC or 1999/45/EC

For the full text of the R phrases mentioned in this Section, see Section 16

2.2 Label elements

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Signal Word

Danger

Hazard Statements

- H314 - Causes severe skin burns and eye damage
- H317 - May cause an allergic skin reaction
- H371 - May cause damage to organs
- H373 - May cause damage to organs through prolonged or repeated exposure
- H410 - Very toxic to aquatic life with long lasting effects

Precautionary Statements - EU (§28, 1272/2008)

- P280 - Wear protective gloves/ protective clothing/ eye protection/ face protection
- P303 + P361 + P353 - IF ON SKIN (or hair): Remove/ Take off immediately all contaminated clothing. Rinse skin with water/shower
- P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
- P310 - Immediately call a POISON CENTER or doctor/ physician
- P280 - Wear eye protection/ face protection
- P260 - Do not breathe dust/fume/gas/mist/vapors/spray

2.3 Other Hazards No information available

Section – 3: Composition / Information on Ingredients

Substances

Ingredients: Active Ingredient - Cinacalcet HCl; Inactive ingredients- Proprietary Information
Chemical Name: N-[1-(R)-(-)-(1-naphthyl)ethyl]-3-[3-(trifluoromethyl)phenyl]-1-aminopropane
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Section – 4: First Aid Measures

Description of first-aid measures

- Eye Contact:** In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
- Skin Contact:** Wash off immediately with soap and plenty of water removing all contaminated clothes and shoes. Consult a physician if necessary.
- Inhalation:** Move to fresh air. If symptoms persist, call a physician.
- Ingestion:** Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person. Consult a physician.
- Notes to Physician:** Treat symptomatically.

Section – 5: Fire Fighting Measures

Extinguishing media

Flammable Properties: No information available.
Extinguishing Media: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: No information available.

5.3 Advice for firefighters

Protective Equipment and Precautions for Firefighters:
As in any fire, wear self-contained breathing apparatus pressure-demand, NIOSH (approved) and full protective gear.

Section – 6: Accidental Release Measures**Personal precautions, protective equipment and emergency procedures**

Spill Procedures: If material is released or spilled, cordon off spill area. Take proper precautions to minimize Exposure by using appropriate personal protective equipment in cleaning up a spill. If in Powder form, wet down spilled material to minimize airborne dispersion. Soak up material with absorbent e.g., paper towels, and wash spill area thoroughly with appropriate cleaning Materials. Dispose of collected material in accordance with applicable waste disposal Regulations. Avoid release to the environment.

Section – 7: Handling and Storage**7.1 Precautions for Safe Handling**

Handling and Storage: Avoid contact with skin, eyes or clothing. Do not eat, drink or smoke in work areas. Use adequate ventilation to minimize exposure. Wash hands, face and other potentially exposed areas immediately after handling this material. Remove contaminated clothing prior to entering eating areas. Clean protective equipment thoroughly after each use. Store in a well ventilated area.

Storage: Keep containers tightly closed in a cool, well-ventilated place

Safe Handling Advice: No information available

Section – 8: Exposure Controls / Personal Protection**8.1 Control parameters**

Occupational Exposure Limit: Please refer to Section 11 for more information. No exposure guidelines established by ACGIH, NIOSH or OSHA. Amgen recommends an occupational exposure limit (OEL) of 30 µg/m³ as an 8-hour time weighted average over a 40-hour work week. The OEL is designed as an acceptable airborne concentration of a substance for which it is believed that workers may be repeatedly exposed day after day without adverse health effects. Cinacalcet HCl has been classified per Amgen's Hazard Classification System as an Occupational Exposure Band 3 compound (20 µg/m³ - 100 µg/m³) with the following suffixes: SENS (sensitizer), EYE (eye damage), and Specific Target Organ Toxicity - Repeated Exposure (STOT-RE) - Category 2 (eye and cecum).

Engineering Controls: When practicable, handle material in enclosed processes or in processes with effective local exhaust ventilation or within a chemical hood.

8.2 Exposure controls**Personal Protective Equipment**

Eye/face Protection: Wear safety glasses with side shields, chemical splash goggles, or safety glasses with side shields and a full-face shield to prevent contact with eyes. The choice of protection should be based on the job activity and potential for exposure to the eyes and face.

Skin Protection: Use gloves or other appropriate personal protective equipment if skin contact with formulation is possible. Wear lab coat or other protective over garment if splashing is possible. The choice of protection should be based on the job activity and potential for skin contact.

Respiratory Protection: When possible, handle material in enclosed processes or containers. If it is properly handled with effective local exhaust ventilation or containment, respiratory protection may not be needed. For procedures involving larger quantities or dust/aerosol generating procedures such as weighing or a large transfer of liquids, an air-purifying respirator with NIOSH approval for dusts and mists may be needed. The choice of protection should be based on the job activity and the potential for exposure.

Other: Wash hands, face and other potentially exposed areas after handling material (especially before eating, drinking or smoking). Clean protective equipment thoroughly after each use.

8.3 Environmental exposure controls

Environmental Exposure Controls Avoid release to the environment. Please refer to Section 12 for more information.

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Section – 9: Physical and Chemical Properties

Appearance	: White to off-white (Cinacalcet HCl)
Physical State	: Solid
Molecular Weight	: 393.87 as the HCl salt
Odor	: No information available
Odor Threshold	: No information available
pH	: 5.1 - pH of aqueous solution (saturated at 25 °C)
Melting Point	: 178-184 °C (Cinacalcet HCl)
Boiling Point	: No information available
Flash Point	: No information available
Evaporation Rate	: No information available
Lower explosive limit	: No information available
Upper explosive limit	: No information available
Vapor Pressure	: No information available
Vapor Density (air = 1)	: Not applicable
Relative density	: No information available
Water Solubility	: Approx. 1,500 mg/L at pH 5; <10 mg/L at pH 7
Partition Coefficient (log Kow)	: Log Pow value 4.79
Viscosity	: No information available

Section – 10: Stability and Reactivity

- 10.1 Reactivity** No information available
10.2 Chemical stability No information available
10.3 Possibility of hazardous reactions No information available
10.4 Conditions to avoid No Information available
10.5 Incompatible materials No information available
10.6 Hazardous decomposition products No information available
10.7 Other information

Dust Explosion Properties: MIE 50-100mJ, Kst Value 256 (tested on Cinacalcet HCL milled granulation), MIE 50-100mJ, Kst Value 224 (tested on Cinacalcet HCL final blend)

Thermal Stability: 123 °C (tested on Cinacalcet HCL milled granulation), 181 °C (tested on Cinacalcet HCL final blend)

Section – 11: Toxicological Information**11.1 Information on toxicological effects Cinacalcet HCl**

Acute Toxicity: Cinacalcet HCl was tested in oral acute rat studies and the LD50 was >1,500 mg/kg body weight. Clinical signs of toxicity at 1500 mg/kg included thin appearance, hyperactivity, staggered gait, hypoactivity, hunched posture and tremors. Based on available data, the GHS classification criteria are not met.

Skin corrosion/irritation: Very slight dermal irritation based on animal studies. Based on available data, the GHS classification criteria are not met.

Serious eye damage/eye irritation: Severely irritating to the eye based on animal studies.

Respiratory or skin sensitization: Mild sensitizer based on animal studies.

Germ cell mutagenicity: Not mutagenic in a battery of in vitro and in vivo studies. Based on available data, the GHS classification criteria are not met.

Carcinogenicity: Did not show tumorigenic effects in animal experiments. Not listed by NTP, IARC, or OSHA as a carcinogen. Based on available data, the GHS classification criteria are not met.

Reproductive toxicity: Not a reproductive toxicant in animals. Did not show teratogenic effects in animal experiments. Based on available data, the GHS classification criteria are not met.

STOT - single exposure: No information available

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STOT - repeated exposure: Cinacalcet HCl was tested in a 26 week oral study in rats and slight to mild hyperplasia or inflammation in the cecum was noted at a dose of 100 mg/kg (these findings were not observed in a 3-month study or carcinogenicity studies). Minimal cataractous changes were observed, predominantly in the 100-mg/kg/day dose group. The NOAEL for this study was 25 mg/kg/day. The NOAEL in a 1 year oral monkey study was 50 mg/kg/day; mild weight loss or decrease in body weight gain accompanied by appetite suppression and soft feces occurred at 100 mg/kg/day.

Aspiration Hazard: No information available

Section – 12: Ecological Information

12.1 Toxicity

Ecotoxicity effects: Cinacalcet HCl is very toxic in acute and chronic studies evaluating its effects on aquatic organisms and invertebrates.

The 96-hour LC50 value in fathead minnow under static conditions for cinacalcet was 0.085 mg/L, with most of the mortality occurring within the first 24 hours. At the lowest concentration tested (0.063 mg/L), 1/20 or 5% of the test animals died at the 96-hour interval. No NOEC was achieved, although the 0.063 mg/L was the EC05 or LOEC for the study. In daphnia magna, the 24-hour and 48-hour EC50 for Cinacalcet HCl are 0.42 mg/L and 0.33 mg/L based on nominal concentrations and 0.23 and 0.16 mg/L based on measured concentrations, respectively. The NOEC was 0.11 mg/L based on nominal concentrations and 0.049 mg/L based on measured concentrations.

An acute algal inhibition study produced the following values:

- 72- and 96-hr EC50 – 0.0191 and 0.0175 mg/L (cell numbers)
- 72- and 96-hour EC50 – 0.0203 and 0.0191 mg/L (area under the growth curve)
- 72- and 96-hour EC50 - 0.0330 and 0.0320 mg/L (growth rates)

In a chronic daphnia reproductive study, the 21-day LC50 for mortality in the parents was 0.14 mg/L. The LOEC and NOEC for parent mortality were 0.20 mg/L and 0.10 mg/L. The LOEC and NOEC for reproductive effects were 0.050 mg/L and 0.025 mg/L, respectively.

- 72- and 96-hour LOEC and NOEC - 0.0250 and 0.0125 mg/L (cell numbers, area under the growth curve and growth rate).

12.2 Persistence and degradability

Persistence/Degradability: Cinacalcet HCl is not considered to be biodegradable based on the results of a screening respirometer test and a sealed vessel CO₂ production test. An aerobic and anerobic biodegradation test in sediment suggests that if cinacalcet gets into the environment, it would irreversibly bind and remain in the sediment.

12.3 Bioaccumulative potential

Bioaccumulation/ Accumulation: In an activated sludge respiratory inhibition study, the 3-hour EC50 and EC20 were 35.6 mg/L and 15.4 mg/L, respectively. The NOEC from the nominal concentration data and effects observed was approximately 1 mg/L.

12.4 Mobility in soil

Mobility in Environmental Media: No information available

12.5 Results of PBT and vPvB assessment

Results of PBT and vPvB assessment: No information available

12.6 Other adverse effects

Other Adverse Effects: No information available

Section – 13: Disposal Considerations

13.1 Waste treatment methods

Waste Disposal Method: Dispose of any waste according to prescribed federal, state, local and competent authority guidelines.

Section – 14: Transport Information

DOT : Not regulated

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IATA**UN-No** UN Number 3077**Proper Shipping Name** Environmentally Hazardous Substance, solid, n.o.s. (Cinacalcet HCl)**Packing Group** Packing Group (PG) III**Section – 15: Regulatory Information****15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture****International Inventories****TSCA:** Not determined**EINECS/ELINCS** -**DSL/NDSL** -**PICCS:** -**ENCS:** -**CHINA:** -**AICS:** -**KECL:** -**Legend****TSCA** - United States Toxic Substances Control Act Section 8(b) Inventory**EINECS/ELINCS** - European Inventory of Existing Commercial Chemical Substances/EU List of Notified Chemical Substances**DSL/NDSL** - Canadian Domestic Substances List/Non-Domestic Substances List**PICCS** - Philippines Inventory of Chemicals and Chemical Substances**ENCS** - Japan Existing and New Chemical Substances**IECSC** - China Inventory of Existing Chemical Substances**AICS** - Australian Inventory of Chemical Substances**KECL** - Korean Existing and Evaluated Chemical Substances**State Regulations****California Proposition 65:** This product does not contain any Proposition 65 chemicals.**15.2 Chemical safety assessment**

No CSA has been conducted

Section – 16: Other Information**Text of R phrases mentioned in Section 2**

R41 - Risk of serious damage to eyes

R43 - May cause sensitization by skin contact

R50 - Very toxic to aquatic organisms

R53 - May cause long-term adverse effects in the aquatic environment

M)SDS revision date : 17/04/2015**(M)SDS revision number:** 01**Disclaimer:** The information above is believed to be accurate and represents the best information currently available to us. Users should make their own investigations to determine the suitability of the information for their particular purposes. This document is intended as a guide to the appropriate precautionary handling of the material by a properly trained person using this product.