1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERSTANDING

1.1 Product identifier
Product Name: Sensipar®
(Cinacalcet HCl)
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

1.2 Relevant identified uses of the substance or mixture and uses advised against
Recommended Use: Pharmaceutical
Uses advised against: No information available

Manufacturer:
Amgen Inc.
One Amgen Center Drive
Thousand Oaks, California  91320-1799
1-805-447-7233
1-805-447-1000

Emergency Telephone Number:
Chemtrec
NORTH AMERICA 1-800-424-9300,
INTERNATIONAL 1-703-527-3887

2. HAZARDS IDENTIFICATION

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Eye Damage / Eye Irritation</td>
<td>Category 1</td>
</tr>
<tr>
<td>Skin Sensitization</td>
<td>Sub-category 1B</td>
</tr>
<tr>
<td>Specific TOST - Repeated Exposure Oral</td>
<td>Category 2 eyes and cecum</td>
</tr>
<tr>
<td>Acute Aquatic Toxicity</td>
<td>Acute 1</td>
</tr>
<tr>
<td>Chronic Aquatic Toxicity</td>
<td>Chronic 1</td>
</tr>
</tbody>
</table>

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
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

### 3. COMPOSITION/INFORMATION ON INGREDIENTS

#### 3.1 Substances

**Ingredients:**
Active Ingredient - Cinacalcet HCl; Inactive ingredients- Proprietary Information

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

**CAS-No:** 364782-34-3
4. FIRST AID MEASURES

4.1 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.

5. FIRE-FIGHTING MEASURES

5.1 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.

6. ACCIDENTAL RELEASE MEASURES

6.1 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.
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
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/m$^3$ 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/m$^3$ - 100 µg/m$^3$) 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.
9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>White to off-white (Cinacalcet HCl)</td>
</tr>
<tr>
<td>Physical State</td>
<td>Solid</td>
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<tr>
<td>Molecular Weight</td>
<td>393.87 as the HCl salt</td>
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<tr>
<td>Odor</td>
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</tr>
<tr>
<td>Odor Threshold</td>
<td>No information available</td>
</tr>
<tr>
<td>pH</td>
<td>5.1 - pH of aqueous solution (saturated at 25 °C)</td>
</tr>
<tr>
<td>Melting Point</td>
<td>178-184 °C (Cinacalcet HCl)</td>
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<tr>
<td>Boiling Point</td>
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<tr>
<td>Flash Point</td>
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<tr>
<td>Evaporation Rate</td>
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</tr>
<tr>
<td>Lower explosive limit</td>
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</tr>
<tr>
<td>Upper explosive limit</td>
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<tr>
<td>Vapor Pressure</td>
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<tr>
<td>Vapor Density (air = 1)</td>
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<tr>
<td>Relative density</td>
<td>No information available</td>
</tr>
<tr>
<td>Water Solubility</td>
<td>Approx. 1,500 mg/L at pH 5; &lt;10 mg/L at pH 7</td>
</tr>
<tr>
<td>Partition Coefficient (log Kow)</td>
<td>Log Pow value 4.79</td>
</tr>
<tr>
<td>Viscosity</td>
<td>No information available</td>
</tr>
</tbody>
</table>

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)
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

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
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

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.

14. TRANSPORT INFORMATION

DOT 
Not regulated

IATA 
UN-No UN Number 3077
Proper Shipping Name Environmentally Hazardous Substance, solid, n.o.s. (Cinacalcet HCl)
Packing Group Packing Group (PG) III
15. REGULATORY INFORMATION

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

International Inventories

<table>
<thead>
<tr>
<th>Legend</th>
<th>Inventory Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSCA:</td>
<td>Not determined</td>
</tr>
<tr>
<td>EINECS/ELINCS</td>
<td>-</td>
</tr>
<tr>
<td>DSL/NDSL</td>
<td>-</td>
</tr>
<tr>
<td>PICCS:</td>
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<td>ENCS:</td>
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<td>CHINA:</td>
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<tr>
<td>AICS:</td>
<td>-</td>
</tr>
<tr>
<td>KECL:</td>
<td>-</td>
</tr>
</tbody>
</table>

State Regulations

California Proposition 65: This product does not contain any Proposition 65 chemicals.

15.2 Chemical safety assessment

No CSA has been conducted.
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

Revision Number: 15

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections, which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it may be biologically active.