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

Product Identifier

Product Name: Ivabradine Tablets, 5 mg and 7.5 mg

Trade Name: Not established

Chemical Name: *2H*-3-Benzazepin-2-one,3-[3-[[[(7*S*)-3,4-dimethoxybicyclo[4.2.0]octa-1,3,5-trien-7- yl]methyl]methylamino]propyl]-1,3,4,5-tetrahydro-7,8-dimethoxy-, hydrochloride (1:1)
(or)
3-[3-({[(7*S*)-3,4-dimethoxybicyclo[4.2.0]octa-1(6),2,4-trien-7-yl]methyl}(methyl) amino)propyl]-7,8-dimethoxy-2,3,4,5-tetrahydro-1*H*-3-benzazepin-2-one, hydrochloride

Product Use: Ivabradine is indicated to reduce the risk of hospitalization for worsening heart failure in adult patients with stable, symptomatic chronic heart failure with reduced left ventricular ejection fraction.

Product Type: Regulatory Prescription Drug

Details of the supplier/manufacture of the Safety Data Sheet:

Manufactured for:
Ingenus Pharmaceuticals, LLC
Orlando, Florida 32811-7193

Manufactured by:
Centaur Pharmaceuticals Private Limited
Plot no. 4, International Biotech Park, Phase-II, Hinjewadi, Pune, Maharashtra 411057, India

Emergency telephone number: 1-866-321-5031

Contact E-Mail: customerservice@ingenus.com

2. HAZARDS IDENTIFICATION

Emergency Overview

Pharmaceutical product intended for clinical and commercial manufacturing purposes only. Product contains an active pharmaceutical ingredient, ivabradine, intended for oral treatment coronary artery disease and chronic heart failure. Effect of lowering of heart rate may occur if exposures repeatedly exceed the Occupational Exposure Limit describe in Section 8. Avoid inhalation, skin contact, eye contact, and accidental ingestion.

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

Acute Oral Toxicity	Category 4
Reproductive Toxicity	Category 1B
Specific TOST - Repeated Exposure Oral	Category 2 Heart
Chronic aquatic toxicity	Chronic 2

2.2 Label elements



Signal Word: **Danger**

SGHH0999
H302 - Harmful if swallowed
H360 - May damage fertility or the unborn child
H373 - May cause damage to organs through prolonged or repeated exposure
H411 - Toxic to aquatic life with long lasting effects

GHSPO642
P201 - Obtain special instructions before use
P202 - Do not handle until all safety precautions have been read and understood
P281 - Use personal protective equipment as required
P308 + P313 - If exposed or concerned: Get medical advice/ attention
P260 - Do not breathe dust/fume/gas/mist/vapors/spray

2.3 Other Hazards: No information available

3. COMPOSITION / INFORMATION ON INGREDIENTS

Ingredients	CAS No.	Chemical Formula
Ivabradine Hydrochloride	130693-82-2	$C_{27}H_{37}ClN_2O_5$
Tablettose 80 Lactose monohydrate	10039-26-7	$C_{12}H_{22}O_{11}$, H_2O
Maltodextrin 334225 L Glucidex IT-19	9050-36-6	Not Available
Maize starch B	9005-25-8	Not Available
Colloidal Silicon Dioxide	7631-86-9	SiO_2
Magnesium Stearate	557-04-0	$C_{36}H_{70}MgO_4$
Opadry II 31F240016 Orange-INH	Not Available	Not Available
Purified water	7732-18-5	H_2O

4. 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: If symptoms persist, call a physician. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person.

Notes to Physician Treat symptomatically.

5. FIREFIGHTING MEASURES

Flammable Properties: No information available.

Extinguishing Media: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Specific Hazards Arising from the substance or mixture

Hazardous Combustion Products: No information available.

Special 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

Precautions for Safe Handling: 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.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

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 7 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. Ivabradine has been classified per Amgen's Hazard Classification System as an Occupational Exposure Band 4 compound (5

	µg/m^3 - 20 µg/m^3) with the following suffixes: A (acute toxicity), R (reproductive and/or developmental effects) Specific Target Organ Toxicity - Repeated Exposure (STOT-RE) Heart
Engineering Controls:	When practicable, handle material in enclosed processes or in processes with effective local exhaust ventilation or within a chemical hood.
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.
Environmental Exposure Controls:	Avoid release to the environment.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	Light salmon colored (tablet)
Molecular Weight:	505.5 Dalton
Odor:	No information available
Odor Threshold:	No information available
pH:	No information available
Melting point (°C) VALUE	192 °C
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:	No information available
Vapor Density (air = 1):	No information available
Relative density:	No information available
Water Solubility:	No information available
Partition Coefficient (log Kow):	2.1 at pH 7.4
Viscosity:	No information available

10. STABILITY AND REACTIVITY

Reactivity: No information available

Chemical Stability: No information available

Possibility of Hazardous Reactions: No information available

Conditions to Avoid: This material will present an explosion and deflagration hazard risk when dispersed and ignited in air. Grounding and bonding of process equipment should be implemented. Consider inerting the process environment to mitigate an explosion hazard. High temperature process environments should be avoided to minimize the risk of a dust cloud explosion. This material is resistive and capable of accumulating a charge during process operations. It is recommended that measures are taken to reduce the rate of charge generation during transport. The rate of charge relaxation should also be increased by using proper bonding and grounding of process equipment.

Incompatible Materials: No information available

Hazardous Decomposition Products: No information available

Other information

Dust Explosion Hazard Properties
MIE: 3mJ < MIE < 10 mJ (Es = 7) without inductance
MIT (dust cloud): 430°C
Kst: 270 bar-m/sec ± 10%
Pmax: 8.3 bar ± 10%
LOC: 10.5 vol % ± 1

Electrostatic Properties
Volume resistivity: 4.3 x 10^{16} Ω-cm
Calculated Dielectric Constant: 3.37
Measured Decay Time: 2523 sec
Tested on the Active Pharmaceutical Ingredient.

11. TOXICOLOGICAL INFORMATION

Information on toxicological effects

Acute Toxicity: Ivabradine oral LD50 in rats is 840 mg/kg (GHS Category 4).

Skin corrosion/irritation: Based on available data, the GHS classification criteria are not met.

Serious eye damage/eye irritation: Based on available data, the GHS classification criteria are not met.

Respiratory or skin sensitization: Based on available data, the GHS classification criteria are not met.

Germ cell mutagenicity: Based on available data, the GHS classification criteria are not met.

Carcinogenicity: Based on available data, the GHS classification criteria are not met.

Reproductive toxicity: Ivabradine oral exposure to pregnant rats and rabbits resulted in embryo-fetotoxicity and teratogenicity (GHS Category 1B).

STOT - single exposure: Based on available data, GHS classification is not possible.

STOT - repeated exposure: Ivabradine main repeated-dose oral toxicity studies were conducted in rats and dogs and the heart was the main target organ. Focal myocardial lesion between 10-100 mg/kg/day in 90-day repeat dose studies in rats (GHS Category 2 - Heart)

Aspiration Hazard: No information available

12. ECOLOGICAL INFORMATION

Toxicity

Ecotoxicity effects:

- Algae Growth Inhibition test, Scenedesmus subspicatus (72 hrs) ErC50 = 14.9 mg/L
- Acute Mobilization test, Daphnia magna (48 hrs) EC50 = 88.6 mg/L
- Acute toxicity on fish, Rainbow Trout, Oncorhynchus mykiss (96 hrs) LC50 > 500 mg/L
- Reproduction test, water flea Daphnia magna (21 days) NOEC = 1.58 mg/L
- Early-life Stage Toxicity on Fish, Rainbow Trout, Oncorhynchus mykiss (64 days) NOEC = 10 mg/L
- Activated sludge test, Respiration inhibition EC50 > 1000 mg/L
- GHS Category Acute 3
- GHS Category Chronic 2

Persistence and degradability

Persistence/Degradability:

- Ready biodegradability test - Approximately 0% degradation over a 28 day test period (does not biodegrade)
- -Water sediment Study - Rapid dissipation from water column:6.9 to 8.6% at day 4,76 to 90% at day 14 in sediment (DT50 sediment > 100 days). No tranformation products > or = 10% or with increasing concentrations

Bioaccumulative potential

Bioaccumulation/ Accumulation:

- N-octanol:water partition coefficient (Log Kow) 2.1 at pH 7.4

Mobility in soil

Mobility in Environmental Media:

- Adsoprtion coefficient (log Koc) 1.34 and 4.00 at pH 1.51 and 10.58, respectively.
- Water Solubility 47 g/L

Results of PBT and vPvB assessment

Results of PBT and vPvB assessment:

- Does not meet criteria of PBT or vPvB compound

Other adverse effects

Other Adverse Effects: No information available

13. DISPOSAL CONSIDERATIONS

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

14. TRANSPORT INFORMATION

DOT: Not regulated by U.S. DOT, IATA, or IMDG.

15. REGULATORY INFORMATION

International Inventories

TSCA:	--
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.
Chemical safety assessment	No CSA has been conducted.

16. OTHER INFORMATION

Revision date:	19-July-2024
Prepared by:	Regulatory and Medical Affairs, Ingenus Pharmaceuticals, LLC

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End of Safety Data Sheet