Hypoxyprobe™-1

[Pimonidazole Hydrochloride]

[CAS# 70132-51-3]

An Investigational New Drug for the detection of tissue hypoxia

Material Safety Data Sheet

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Material Safety Data Sheet

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Section 1 - Product and Company Information

Substance Name	Pimonidazole Hydrochloride
Brand Name	Hypoxyprobe™-1
Company	Hypoxyprobe, Inc (HPI)
Street Address	121 Middlesex Turnpike
City, State, Zip, Country	Burlington, MA 01803, USA
Technical Phone:	780-994-8725 or 781-272-6888
Fax	781-272-9288
e-mail	tlee@natural-pharma.com

Section 2 – Composition/Information on Ingredients

Substance Name	Pimonidazole hydrochloride
CAS #	70132-51-3
SARA 313 listed:	No
Formula	$C_{11}H_{19}N_4O_3Cl$
Synonyms	1-[(2-hydroxy-3-piperidinyl)propyl]-2-nitroimidazole hydrochloride; Ro 03-8799 hydrochloride salt; Hypoxyprobe™-1.

Section 3 – Hazards Identification

Emergency Overview

Toxic (USA) Harmful (EU).

Harmful to humans if swallowed in quantities exceeding 0.75 gm/m^2

For additional information on toxicity, please refer to Section 11.

Section 4 – First Aid Measures

Oral Exposure
If swallowed in amounts exceeding 0.75 g/m^2, wash out mouth with water provided person is conscious. Call a physician.

Inhalation Exposure
If inhaled, remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen.

Dermal Exposure
In case of contact, immediately wash skin with soap and copious amounts of water.

Eye Exposure
In case of contact, immediately flush eyes with copious amounts of water for at least 15 minutes.

Section 5 – Fire Fighting Measures

Autoignition Temp: Not known

Flammability: Not flammable

Firefighting Protective Equipment: Wear protective clothing to prevent contact with body.

Exposure Hazard(s) Low toxicity, non-hazardous. Toxicity develops at dosages that exceed 0.75 gm/m^2 administered daily for 20 days.

Section 6 – Accident Release Measures

Procedure(s) of Personal Precaution(s)

Wear gloves.

Methods for Cleaning Up

Sweep up, place in a bag and hold for waste disposal. Avoid raising dust. Ventilate area and wash spill site after material pickup is complete.

Section 7 – Handling and Storage

Handling: User Exposure

Non-hazardous but avoid unnecessary contact. Do not get in eyes, on skin, on clothing.

Storage

Keep tightly closed. Store in a cool dry place under conditions of subdued light.

Section 8 – Exposure Controls/PPE

Engineering Controls: Safety shower and eye bath.

Personal Protective Equipment

Hand: Gloves.
Eye: Chemical safety goggles.

General Hygiene Measures: Wash after handling.
Wash contaminated clothing before reuse.

Section 9 – Physical/Chemical Properties

Appearance
Color: Light beige
Form: Fine crystals
Molecular Weight: 290.17 AMU

Section 9 – Physical/Chemical Properties (cont'd)

Property	Value
pH	1 gm dissolved in 100 ml saline has pH of 3.9 ± 1
BP/BP Range	Not applicable
MP/MP Range	Decomposes > 120°C
Freezing Point	Not applicable
Vapor Pressure	Not available
Vapor Density	Not available
Saturated Vapor Conc.	Not available
SG/Density	Not available
Bulk Density	Not available
Odor Threshold	Odorless
Volatile %	Not available
VOC Content	Not available
Water Content	2.2 %
Solvent Content	< 1%
Evaporation Rate	Not available
Viscosity	Not applicable
Partition Coefficient	8.5 for free base in octanol/water.
Decomposition Temp.	Decomposes > 120°C.
Flash Point °F	Not flammable
Flash Point °C	Not flammable
Explosion Limits	Not flammable
Autoignition Temp	Not flammable
Solubility	116 g/L in H_2O

Section 10 – Stability and Reactivity

Stability: Highly stable as solid or aqueous solution when stored at 4°C in the absence of light.

Materials to Avoid: Strong oxidizing agents: strong illumination; strong alkali

Hazardous Decomposition Products: Carbon monoxide, Carbon dioxide, Nitrogen oxides.

Section 11 – Toxicological Information

Route of Exposure

Multiple Routes: Harmful if swallowed, inhaled, or absorbed through skin in high dosages

Toxicity Data and Signs and Symptoms of Exposure:

Mice

LD50/7days in mice: 728 mg/kg (Walton et al, Br. J. Cancer 59(5): 667-675, 1989).

LD50/2days in mice: 680 mg/kg (Stone et al, Int. J. Radiat. Oncol. Biol. Phys. 12:1097-1100, 1986).

These results indicate that pimonidazole HCl is non-hazardous in the hands of trained laboratory or clinical personnel.

Rats and non-human primates

In a 28-day toxicity study, intravenous pimonidazole hydrochloride doses of 50, 120 and 300 mg/kg/day were administered in three study groups of cynomolgus monkeys (long-tailed macaque; Macaca fascicularis) for 10 days. At this time, liver function tests revealed liver damage in some of the monkeys that were receiving 300mg/kg/day. One monkey in this group died and post mortem histological investigation revealed acute liver damage. The daily dosage of pimonidazole hydrochloride was decreased from 50, 120 and 300 mg/kg/day to 33, 80 and 200 mg/kg/day, respectively, in the three study groups. Liver function tests returned to control levels in the ensuing 18 days of daily 200 mg/kg/day dosage in the monkeys that had initially received 300 mg/kg/day. There was no functional or histological evidence of liver damage at the end of 28 days for monkeys in any of the study groups. There was no evidence of hepatotoxicity in rats dosed with pimonidazole hydrochloride in a manner similar to that used for monkeys. In monkeys, there was no adverse effect on spermatogenesis in any of the study groups but some salivation was noted in monkeys receiving 80 and 200 mg/kg/day for 28 days. Muscle tremor and vomiting were observed occasionally in the 200mg/kg/day group of monkeys. Some locomotor disturbances lasting a few minutes to several hours were seen in rats receiving 200 mg/kg/day.

Humans

The single dose of 0.5 gm/m^2 of pimonidazole hydrochloride used for tumor hypoxia measurement in humans is equivalent to approximately 13 mg/kg and, therefore, far below the dose of 300 mg/kg/day for 10 days that appears to be near the threshold for liver damage in primates. Although pimonidazole hydrochloride, like many 2-nitroimidazole drugs, is toxic to hypoxic cells, pimonidazole hydrochloride is not toxic to hypoxic cells at the concentrations used for hypoxia marking in animals or humans.

When injected intravenously in humans, doses that exceed 0.75 gram /meter squared can produce diarrhea, vomiting, skin rash, sweating, disorientation and feelings of malaise and heat. Ingestion of total doses that exceed 1.0 gram/meter squared (typically 0.75 – 1.0 grams total) are likely to have similar central nervous toxicities. Total doses equal to or greater than 5.0 grams can induce transient coma but no long-term toxic sequelae are expected even at this high dose.

Section 12 – Ecological Information

Not available

Section 13 – Disposal Considerations

Appropriate Method of Disposal of Substance or Preparation

Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber. Observe all federal, state, and local environmental regulations.

Section 14 – Transport Information

DOT

Proper Shipping Name: Organic, n.o.s.

Packing Group: Packing Group III

UN Not dangerous; not hazardous; no UN number assigned

Section 15 – Regulatory Information

US Classification and Label Text

Indication of Danger
Toxic (USA) Harmful (EU).

Risk Statements
Harmful if swallowed in large quantity.

Safety Statements
In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
Wear suitable protective clothing.

United States Regulatory Information
SARA 313 Listed: No

Section 16 – Other Information

Warranty

The above information is believed to be correct but does not purport to be all-inclusive and shall be used only as a guide. Neither NPI Inc. nor HP, Inc. shall not be held liable for any damage resulting from handling or from contact with the above product.