Hypoxyprobe™-1

[Pimonidazole Hydrochloride]

[CAS# 70132-50-2]

An Investigational New Drug for the detection of tissue hypoxia

Material Safety Data Sheet

Updated 2019

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Section 1 - Product and Company Information

Product 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:	781-272-6888
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e-mail	tlee@natural-pharma.com

Section 2 – Composition/Information on Ingredients

Substance Name	Pimonidazole hydrochloride
CAS #	70132-50-2
SARA 313 listed:	No
Formula	$C_{11}H_{19}N_40_3Cl$
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 if swallowed in quantities exceeding 0.5 gm/m2.
For additional information on toxicity, please refer to Section 11

Section 4 – First Aid Measures

Oral Exposure
If swallowed, 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: N/A

Flammability: N/A

Extinguishing Media

Suitable: Water spray. Carbon dioxide, dry chemical powder, or appropriate foam.

Firefighting

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

Exposure Hazard(s)

Material: **Low toxicity.** Toxicity develops at dosages that exceed 0.5 gm/m2 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

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	N/A
BP/BP Range	N/A
MP/MP Range	N/A
Freezing Point	N/A
Vapor Pressure	N/A
Vapor Density	N/A
Saturated Vapor Conc.	N/A
SG/Density	N/A
Bulk Density	N/A
Odor Threshold	N/A
Volatile %	N/A
VOC Content	N/A
Water Content	N/A
Solvent Content	N/A
Evaporation Rate	N/A
Viscosity	N/A
Partition Coefficient	8.5 for free base in octanol/water system.
Decomposition Temp.	N/A
Flash Point ^{o}F	N/A
Flash Point ^{o}C	N/A
Explosion Limits	N/A
Autoignition Temp	N/A
Solubility	400 millimolar in aqueous solution

Section 10 – Stability and Reactivity

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

Materials to Avoid: Strong oxidizing agents: strong illumination

Hazardous Deat 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: 667-675, 1989).

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

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 gram 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 applicable.

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

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. NPI Inc. shall not be held liable for any damage resulting from handling or from contact with the above product.