SAFETY DATA SHEET

Pantoprazole Sodium for Injection

1) PRODUCT AND COMPANY IDENTIFICATION

Product Identifier
Product Name: Pantoprazole Sodium for Injection
Common/Trade Name: Protonix IV
Chemical Name: Sodium 5-(difluoromethoxy)-2-[[(3,4-dimethoxy-2- pyridinyl)methyl]sulfinyl]-1H-benzimidazole
Chemical Family: Proton pump inhibitor

Product Use
Pharmaceutical; Used to inhibit gastric acid secretion / Regulated prescription drug
Container Type: Vial

Manufacturer
Piramal Critical Care, Inc
268 Brodhead Road
Bethlehem, PA 18017

Emergency Telephone Number
Customer Service: 610-974-9760 x510
E-Mail: pcccustomerconnect@piramal.com
Emergency Number: CHEMTREC 1-800-424-9300

2) HAZARDS IDENTIFICATION

Classification of the substance or mixture

Classification according to Regulation (EC) No 1272/2008 [CLP]	Classification Procedure
Reproductive toxicity, Category 2	Based on animal data.
Skin sensitization, Category 1	Based on animal data.
Acute oral toxicity, Category 4	Based on animal data.
Acute aquatic toxicity, Category 3	Based on animal data.

Label Elements
Labelling according to Regulation (EC) 1272/2008 :

Signal Word (CLP): Danger, Warning
Hazard Statements (CLP): H361- Suspected of damaging fertility or the unborn child

H317-May cause an allergic skin reaction

H302-Harmful if swallowed

H402 - Harmful to aquatic life

Precautionary Statements (CLP):

P308 + P313 – IF exposed or concerned: Get medical advice/ attention.

P201 – Obtain special instructions before use

P202 – Do not handle until all safety precautions have been read and understood.

P264 – Wash thoroughly after handling.

P273 - Avoid release to the environment

P280 – Wear protective gloves/protective clothing/eye protection/face protection/hearing protection.

P405: Store locked up.

P501: Dispose the contents/container to a special waste collection point (according to the respective local/regional/national/international regulations)

Other Hazards
None.

3) COMPOSITION/INFORMATION ON INGREDIENTS

Substances

Hazardous ingredients according to Regulation (EC) No 1272/2008 and Directive 1999/45/EC

Substance Name	*CAS No.*	*EU/EINECS/ELINCS*	*GHS Classification*	*%*
Pantoprazole Sodium	138786-67-1	Not Listed	Reproductive toxicity, Category 2 H361- Suspected of damaging fertility or the unborn child Skin sensitization, Category 1 H317-May cause an allergic skin reaction Acute oral toxicity, Category 4) H302-Harmful if swallowed Acute aquatic toxicity: Category 3 H402 - Harmful to aquatic life	40 mg

Substance Name	CAS No.	EU/EINECS/ELINCS	GHS Classification	%
Disodium edetate	6381-92-6	613-386-6	Not Listed	1 mg
Sodium hydroxide	1310-73-2	923-604-4/688-015-4/215-185-5	Not Listed	q.s. for pH adjustment
Water for injection	7732-18-5	231-791-2/686-299-4	Not Listed	N/A

4) FIRST AID MEASURES

Description of First Aid Measures

General Advice	Immediately consult a physician. Show this safety data sheet to the doctor in attendance.
Inhalation	Assure fresh air breathing. If you feel unwell, seek medical advice.
Skin Contact	Remove affected clothing and wash all exposed skin area with mild soap and water, followed by water rinse
Eye Contact	Rinse immediately with plenty of water. Obtain ophthalmologist attention if pain, blinking, tears or redness persist.
Ingestion	Rinse mouth with water. Consult a physician

Most important symptoms and effects, both acute and delayed
See Section 11 Information on toxicological effects.

Indication of any immediate attention and special treatment needed
See Section 11 Information on toxicological effects

5) FIRE FIGHTING MEASURES

Extinguishing Media
Suitable Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.
Unsuitable Extinguishing Media: Do not use a heavy water stream. Use of heavy stream of water may spread fire.

Special Hazards Arising from the Substance or Mixture
No data available

Advice for Firefighters
Use self-contained breathing apparatus if necessary

6) ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures
Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions
Place waste in an appropriately labelled, sealed container for disposal. Care should be taken to avoid environmental release.

Methods and Material for Containment and Cleaning Up
Pick up and arrange disposal without creating dust. Put into appropriated container. Dispose of container in accordance with local/regional/national/international regulation.

Reference to Other Sections
See sections 8. Exposure controls and personal protection. See Section 13, Disposal Considerations.

7) HANDLING AND STORAGE

Precautions for Safe Handling
When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Minimize dust generation and accumulation. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste and waste disposal measures to prevent occupational exposure or environmental releases.
Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls. Avoid inhalation. Avoid skin and eye contact.
Ensure there is ready access to an emergency shower.

Conditions for Safe Storage, Including Any Incompatibilities
Store locked up. Keep only in the original container. Keep container tightly closed, in a cool, well-ventilated place. Keep containers upright. Protect containers from damage. For precautions see section 2.

Specific End Use(s)
Apart from the uses mentioned in section 1 no other specific uses are stipulated.

8) EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters

Pantoprazole Sodium	NORMON OEL TWA 8 h	33 mcg/m3
Disodium edetate	DNEL Workers inhaled	Acute local effects; 3 mg/m3 Long-term local effects; 1.5 mg/m3
Sodium hydroxide	OSHA PEL	Ceiling: 2 mg/m3 TWA: 2 mg/m3

Exposure Controls
Engineering controls should be used as the primary means to control exposures. Keep airborne contamination levels below the exposure limits listed above in this section. It is recommended that all operations be fully enclosed and no air recirculated. Ensure there is ready access to an emergency shower.

Personal Protective Equipment:

Working protective equipment	Protective clothing should be specifically selected depending on quantity of substance handled. Chemically resistant boots or shoe covers may be required when working with large quantities of chemicals and the potential exists for large spills to occur. Assessment of the level of risk depends on how the substance will be used.
Respiratory protection	Whenever excessive air contamination (dust, mist, vapor) is generated, respiratory protection, with appropriate protection factors, should be used to minimize exposure. Under normal conditions of use, if the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL. A P3

	filter should be used. Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.
Hand protection	Safety gloves: Latex or nitrile. Latex gloves typically offer sufficient protection when handling small quantities or diluted chemicals with a low chance for contact or splash.
Eye protection	Safety glasses
Skin protection	In small-scale or laboratory operations, lab coats or equivalent protection is required. Disposable garment or other dust impermeable suit should be considered based on procedure or level of exposure.
Environment exposure controls	Comply with the environmental local regulation currently in force.

9) PHYSICAL AND CHEMICAL PROPERTIES

Information on Basic Physical and Chemical Properties

Appearance	A white to off white freeze-dried powder
Odor	Odorless
Odor threshold	No data available
pH	9-10.5
Melting point	No data available
Initial boiling point / boiling range	No data available
Flash point	No data available
Evaporation rate	No data available
Flammability (solid, gas)	No data available
Upper/lower flammability or explosive limits	No data available
Vapor pressure	No data available
Vapor density	No data available
Relative density	No data available
Solubility	Freely soluble in water
Partition coefficient (n-octanol/water)	No data available
Autoignition temperature	No data available
Decomposition temperature	No data available
Viscosity	No data available
Explosive properties	No data available
Oxidizing properties	No data available

Other Information
No data available

10) STABILITY AND REACTIVITY

Reactivity: Stable under recommended storage conditions.
Chemical Stability: Stable under recommended storage conditions
Possibility of Hazardous Reactions: No data available.
Conditions to Avoid: No data available.
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers
Hazardous Decomposition Products: No data available.

11) TOXICOLOGICAL INFORMATION

Information On Toxicological Effects

General Information	The information included in this section describes the potential hazards of the individual ingredients.
Short Term	May be harmful if swallowed. (based on animal data). Accidental ingestion may cause effects similar to those seen in clinical use
Long Term	See known clinical effects below
Known Clinical Effects	Adverse effects most commonly reported in clinical use include headache, diarrhea, nausea, and flatulence. May cause mild skin rash.

Specific target organ toxicity (single exposure)

Animal data

Pantoprazole Sodium
Rat Oral LD50 747 mg/kg
Mouse Oral LD 50 > 1000 mg/kg

Disodium edetate
Rat Oral LD50 2,000 mg/kg
Mouse Oral LD50 2,050 mg/kg
Rabbit Oral LD50 2,300 mg/kg

Sodium hydroxide
Mouse Intraperitoneal LD50 40 mg/kg

Human data
Some reports of overdosage with pantoprazole have been received. No consistent symptom profile was observed after ingestion of high doses of pantoprazole.

Other information
Assessment / Classification: H302-Harmful if swallowed (Pantoprazole Sodium)

Skin corrosion/irritation

Disodium edetate
No classifiable skin or eye irritation could be observed in test on rabbits

Sodium hydroxide
According to the CLP Regulation Annex VI Table 3.1, the concentration limit for corrosivity of NaOH is considered to be 2%. Up to the most recent ATP, this has not been changed.

Other information
Assessment / Classification: Based on available data, the classification criteria are not met.

Serious eye damage/irritation

Disodium edetate
No classifiable skin or eye irritation could be observed in test on rabbits.

Sodium hydroxide
According to the CLP Regulation Annex VI Table 3.1, the concentration limit for corrosivity of NaOH is considered to be 2%. Up to the most recent ATP, this has not been changed.

Other information
Assessment / Classification: Based on available data, the classification criteria are not met.

Respiratory or skin sensitization

Pantoprazole Sodium
Five cases of occupational airborne contact dermatitis caused by lansoprazole, pantoprazole, and omeprazole in pharmaceutical industry workers have been reported so far.
It was published a large study involving 96 workers who reported possible allergic symptoms resulting from occupational exposure to omeprazole during the manufacturing process. Part of the patients underwent patch test and lymphocyte transformation test (LTT) which associated and confirmed allergy in 40 % of patients. The authors also confirmed the relevant sensitizing capacity of omeprazole by performing a predictive test on guinea pigs as previously demonstrated. Indeed, PPIs, among the numerous azole derivatives, are considered to be strong sensitizers via topical exposure. In contrast, oral or systemic exposure is less frequently associated to the development of eczematous symptoms. Therefore, direct contact of PPI formulation with the skin should be avoided.

Disodium edetate
Two studies on dogs with airway hyperresponsiveness using Na2EDTA have been performed. In those dogs bronchoconstriction can be induced. However, considering the fact that no adverse acute or chronic respiratory health effect was reported in workers exposed to Na4EDTA or edetic acid, these results do not warrant a labeling according to EU or GHS criteria.

Sodium hydroxide
Based on a study with male volunteers sodium hydroxide has no skin sensitisation potential.

Other information
Assessment / Classification: H317-May cause an allergic skin reaction (Pantoprazole Sodium)

CMR effects (carcinogenity, mutagenicity and toxicity for reproduction)

Pantoprazole Sodium
Pantoprazole was studied in several mutagenicity studies: Pantoprazole was found negative in the Ames test, an in vivo chromosome aberration assay in rat bone marrow, a mouse lymphoma test, two gene mutation tests in Chinese hamster ovary cells in vitro, and two micronucleus tests in mice in vivo.

Disodium edetate
Na salts of EDTA were tested negative in several Ames tests. Na salts of EDTA were tested negative in several mouse lymphoma assays. Only one mouse lymphoma assay using edetic acid was positive. However, it was not clear whether this effect was due to the test substance or the pH change.

Sodium hydroxide
Both the in vitro and the in vivo genetic toxicity test indicated no evidence for a mutagenic activity.

Other information
Assessment / Classification: Based on available data, the classification criteria are not met.

Carcinogenicity

Pantoprazole Sodium
A slight increase in neoplastic changes of the thyroid was observed in rats receiving pantoprazole at 200 mg/kg/day. The incidences of these tumours were within the historical control ranges for this rat strain. No thyroid neoplasms were observed in the 12-month study. The no-effect dose for both male and female rats is 50 mg/kg, which is 100 times the most commonly used human dose (i.e. 40 mg dose). The effect of pantoprazole on the thyroid is secondary to the effects on liver enzyme induction, which lead to enhanced metabolism of thyroid hormones in the liver. As a consequence, increased TSH is produced, which has a trophic effect on the thyroid gland. Clinical studies have demonstrated that neither liver enzyme induction nor changes in thyroid hormonal parameters occur in man after therapeutic doses of pantoprazole.

Tumours induced in rats and mice by pantoprazole were the result of nongenotoxic mechanisms which are not relevant to humans. Tumours were induced in rodents at dosages that provide higher exposure than with human therapeutic use. Based on kinetic data, the exposure to pantoprazole in rats receiving 200 mg/kg was 22.5 times higher than that found in humans receiving 40 mg oral doses. In mice receiving 150 mg/kg, exposure

to pantoprazole was 2.5 times higher than that in humans.

Disodium edetate
A standard carcinogenicity study on mice and rats using Na3 EDTA did not demonstrate that the test substance is carcinogenic in experimental animals.

Sodium hydroxide
Lack of positive in vitro and in vivo mutagenicity data support no classification for carcinogenicity and support no additional animal testing to assess carcinogenicity.

Other information
Assessment / Classification: Based on available data, the classification criteria are not met.

Reproductive toxicity

Pantoprazole Sodium

Pantoprazole was not teratogenic to rats or rabbits at doses up to 450 and 40 mg/kg/day (gavage), 20 and 15 mg/kg/day (IV injection), respectively.

Treatment of male rats with pantoprazole up to 500 mg/kg PO for 127 days did not affect fertility. Treatment of pregnant rats induced dose-dependent fetotoxic effects: increased pre- and postnatal deaths (450 mg/kg/day), reduced fetal weight and delayed skeletal ossification (150 mg/kg/day), and reduced pup weight (15 mg/kg/day). These results may be explained by maternal toxicity of pantoprazole at high dose and/or placental transfer of pantoprazole.

Disodium edetate

No test substance specific adverse effects were seen on fertility, reproductive performance and developmental toxicity which justify a classification according to Regulation (EC) No 1272/2008.

Sodium hydroxide

NaOH is not expected to be systemically available in the body under normal handling and use conditions and for this reason it can be stated that the substance will not reach the foetus nor reach male and female reproductive organs.

Other information

Assessment / Classification: H361- Suspected of damaging fertility or the unborn child (Pantoprazole Sodium)

Specific target organ toxicity (repeated exposure).
Pantoprazole Sodium
1 Year(s) Rat Oral 300 mg/kg/day LOEL Thyroid
1 Year(s) Dog Oral 60 mg/kg/day LOEL Thyroid

Disodium edetate
90-day study with Na2H2EDTA as well as 2 years feeding studies with Na3EDTA on rats and mice provide reliable toxicological information for an overall NOAEL of about 500 mg/kg bw.

Sodium hydroxide
Oral studies with high concentrations of the substance are corrosive or irritating, while at low concentrations the hydroxide will be neutralized in the

stomach by gastric juice, which has a very low pH. Furthermore it should
be realized that oral exposure to NaOH is negligible under normal handling and use conditions.

Other information
Assessment / Classification: Based on available data, the classification criteria are not met.

12) ECOLOGICAL INFORMATION

Toxicity

Pantoprazole sodium
Pseudokirchneriella subcapitata (Green Alga) OECD EC50 72 Hours 48 mg/L
Daphnia magna (Water Flea) OECD EC50 48 Hours >95 mg/L
Pimephales promelas (Fathead Minnow) OECD LC50 96 Hours >95 mg/L
Activated sludge OECD EC50 3 Hours > 1000 mg/L

Disodium edetate
No acute aquatic toxicity was observed below 100 mg/L for fish, invertebrates and algae. Valid chronic data are available for all trophic levels showing no effect values below 1 mg/L.

Sodium hydroxide
The available data indicate that NaOH concentrations of 20 to 40 mg/L may be acutely toxic to fish and invertebrates (single species tests). Data on pH increases due to the addition of these amounts of NaOH in the used test waters are lacking. In waters with a relatively low buffering capacity, NaOH concentrations of 20-40 mg/L may result in a pH increase with one to several pH units. The high water solubility and very low vapour pressure indicate that NaOH will be found predominantly in water. In water (including soil or sediment pore water), NaOH is present as the sodium ion (Na^+) and hydroxyl ion (OH^-), since solid NaOH rapidly dissolves and subsequently dissociates in water. If emitted to surface water, sorption to particulate matter and sediment will be negligible and so it will not accumulate in living tissues.

Persistence and degradability
Disodium edetate
Disodium dihydrogen ethylenediaminetetraacetate (CAS No. 139-33-3) is not considered to be readily biodegradable.

Bioaccumulative potential
Pantoprazole sodium
Predicted 7.4 Log P 2.05
Sodium hydroxide
Based on the results of the ecotoxicity studies, its dissociation in the environment and lack of bioaccumulation NaOH is not classified for the environmental compartment.

Mobility in soil
No data available.

Results of PBT and vPvB assessment
H402 - Harmful to aquatic life (Pantoprazole sodium)

Other adverse effects
No data available

13) DISPOSAL CONSIDERATIONS

Waste treatment methods
Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases.

This may include destructive techniques for waste and wastewater.

14) TRANSPORT INFORMATION

UN number
Not applicable.

UN proper shipping name
Not applicable.

Transport hazard class(es)
Not applicable.

Packing group
Not applicable.

Environmental hazards
Not applicable.

Special precautions for user
Not applicable.

Transport in bulk according to Annex II of Marpol 73/78 and IBC Code
Not applicable.
Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15) REGULATORY INFORMATION

This safety data sheet complies with the requirements of Regulation (EC) No. 2015/830.
Schedules of Toxic Chemicals and Precursors: Neither banned nor restricted
Restrictions on the marketing and use of certain dangerous substances and preparations: Neither banned nor restricted.
Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals: Neither banned nor restricted
REACH - Candidate List of Substances of Very High Concern for Authorization (Article 59).: This product does not contain substances of very high concern (Regulation (EC) No 1907/2006 (REACH), Article 57).

Safety, health and environmental regulations/legislation specific for the substance or mixture
No data available.

Chemical Safety Assessment
No data available.

16) OTHER INFORMATION

Abbreviations and acronyms
Not applicable.

Training advice
Chemical incident response training.
Chemical hazard awareness training, incorporating labelling, Safety Data Sheets (SDS), Personal Protective Equipment (PPE) and hygiene.
Use of personal protective equipment, covering appropriate selection, compatibility, breakthrough thresholds, care, maintenance, fit and standards.

Classification for mixtures and used evaluation method according to regulation (EC) 1207/2008 [CLP]
Reproductive toxicity, Category 2
Skin sensitization, Category 1
Acute oral toxicity, Category 4
Acute aquatic toxicity: Category 3

Relevant R-, H- and EUH-phrases (number and full text)
Hazard statements:
H361- Suspected of damaging fertility or the unborn child
H317-May cause an allergic skin reaction
H302-Harmful if swallowed
H402 - Harmful to aquatic life
Precautionary statements:
P308 + P313 – IF exposed or concerned: Get medical advice/ attention.
P201 – Obtain special instructions before use.
P202 – Do not handle until all safety precautions have been read and understood.
P264 – Wash … thoroughly after handling.
P273 - Avoid release to the environment
P280 – Wear protective gloves/protective clothing/eye protection/face protection/hearing protection/…
P405: Store locked up.
P501: Dispose the contents/container to a special waste collection point (according to the respective local/regional/national/international regulations)

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SDS Updates:
08-14-2023 – New Document