SAFETY DATA SHEET

1. Identification

Product name: Kengreal™

Synonyms: Cangrelor, Kengrexal™, AR-C69931MX, 3312.F

National Drug Code Number:

65293-003-01	Kengreal 50mg Single Vial
65293-003-10	Kengreal 50mg 10 Count

Recommended uses of the substance or mixture: P2Y12-receptor antagonist; intravenous anti-platelet drug.

Recommended restrictions on use: Do not take internally unless instructed by a physician.

DISTRIBUTOR:
Chiesi USA, Inc.
1255 Crescent Green Drive, Suite 250
Cary, NC 27518

CONTACT INFORMATION:
Telephone: (888) 466-6503
Facsimile: (877) 302-1743
Emergency: (888) 661-9260

2. Hazardous Identification

Note:
- *This product is exempt from hazard communication requirements - product regulated as a drug.*
- *This document provided upon request for those entities in the supply chain that prefer to have SDS for all substances and mixtures, including those for which there is no legal obligation to provide an SDS.*
- *Patients seeking additional information about this product should consult the package insert or their physician, for use-information.*

Classification of the substance or mixture: Target organ systemic toxicity (single exposure) - Category 2

Signal Word: Warning

Pictograms:

Hazard Statements: H371 - May cause damage to circulatory system

Precautionary Statements:

P260 - Do not breathe dust/fume/gas/mist/vapors/spray.

P264 - Wash hands thoroughly after handling.

P270 - Do not eat, drink or smoke when using this product.

Primary route(s) of entry: May be absorbed by inhalation, ingestion, or contact with skin or mucous membranes.

3. Composition/Information on Ingredients

Chemical characterization: Mixture

Hazardous components:

CAS Number	Hazardous Ingredient	Concentration
163706-36-3	Cangrelor Tetrasodium	20-22%

Balance is non-hazardous excipients

4. First Aid Measures

Immediate Medical Attention Needed: Yes

Eye Contact: If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.

Skin Contact: Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.

Inhalation: Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.

Ingestion: If swallowed, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.

Note to Physician: Medical conditions aggravated by exposure: Cangrelor is an anti-platelet agent and may cause effects on the blood (e.g., bleeding). Seek immediate medical attention if any of these signs of very serious bleeding occur: chest pain, vision problems, confusion, slurred speech, weakness on one side of the body. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the manufacturer for potential drug interactions.

5. Fire Fighting Measures

Flammability/Explosivity: No explosivity or flammability data identified. High concentrations of finely divided airborne organic particles can potentially explode if ignited.

Extinguishing Media: Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.

Fire Fighting Instructions: Wear full protective clothing and a self-contained breathing apparatus with a full face piece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

Extinguishing Media: No information identified. May emit toxic fumes of carbon monoxide, carbon dioxide, oxides of nitrogen, and compounds containing chlorine, fluorine, phosphorus, and sulfur.

6. Accidental Release Measures

Personal Protection: If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated.

Spill Cleanup Methods: For small spills, soak up material with absorbent, *e.g.* paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Wash spill area thoroughly with water. Collect spilled material, absorbent and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13).

Environmental Precautions: Do not empty into drains. Avoid release to the environment.

7. Handling and Storage

General Handling: Avoid contact with eyes, skin and other mucous membranes. Wash thoroughly after handling.

Storage Conditions: Store at 15º-30ºC.

8. Exposure Controls/Personal Protection

Exposure Limit Values: There are no OEL entries in this MSDS

DNELs/PNECs: None identified.

Exposure/Engineering Controls : Control exposures to below the OEL (if available). Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at dust generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling of powders. High-energy operations such as milling, particle sizing, spraying or fluidizing should be done within an approved emission control or containment system.

Respiratory protection: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly fitted air-purifying respirator with HEPA filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a powered air-purifying respirator equipped with HEPA filters or combination filters or a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known or in any other circumstances where a lower level of respiratory protection may not provide adequate protection.

Hand protection: Wear nitrile or other impervious gloves if skin contact is possible. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Skin protection: Wear appropriate gloves, lab coat, or other protective over-garment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

Eye protection: Wear safety glasses with side shields if eye contact is likely. *e.g.*, during cleanup of large spill. Base the choice of protection on the job activity and potential for contact with eyes and face.

Other protective measures: Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (*e.g.* in common areas or out-of-doors). Decontaminate all protective equipment following use.

Environmental exposure controls: In case of spill, do not release to drains. Avoid release to the environment.

9: Physical and Chemical Properties

Physical form/Appearance: White to off white powder
Color: White to off-white
Odor: No information identified.
Odor threshold: No information identified.
pH: Approximately 8.5 in aqueous solution.
Taste: No information identified.
Boiling point/boiling range: Not applicable
Melting point/melting range: No information identified.
Flash point: No information identified.
Evaporation rate: No information identified.
Flammability (solid, gas): No information identified.
Explosive Properties: No information identified.
Upper/lower flammability or explosive limits: No information identified.
Oxidizing properties: No information identified.
Vapor pressure: No information identified
Molecular Weight: 864.3(as sodium salt)
Molecular Formula: $C_{17}H_{21}N_5Cl_2F_3Na_4O_{12}P_3S_2$
Density: No information identified.
Specific Gravity: No information identified.
Viscosity: No information identified.
Water solubility: Soluble
Solvent solubility: No information identified.
Autoflammability: No information identified.
Partition coefficient ***(n-octanol/water)*** **:** No information identified.
Vapor density: No information identified.
Relative Density: No information identified.
Auto Ignition temperature: No information identified.
Decomposition Temperature: No information identified.

10: Stability and Reactivity

Reactivity: No information identified.

Chemical stability: No information identified.

Conditions to avoid: Avoid extreme temperatures. See Section 7 for appropriate storage conditions.

Materials to avoid/incompatible materials: No information identified.

Hazardous decomposition products: No information identified.

Hazardous polymerization: Not expected to occur.

11. Toxicological Information

Routes of entry: May be absorbed by inhalation, skin contact and ingestion.
Acute Toxicity:

Compound	Type	Route	Species	Dose
Cangrelor	Min. lethal dose	IV	Rat	300 mg/kg
	Min. lethal dose	IV	Mice	240 mg/kg

Additional Acute Toxicity: In three day toxicity studies in rats, doses of 25 mg/kg/day were associated with minor signs of toxicity. Doses of 105 mg/kg/day were associated with changes in plasma and urine chemistry, indicating effects on the kidney and possibly the liver.

Irritation/Corrosion: No data available.

Sensitization: No data available.

Repeat Dose Toxicity: Rat, 28-day IV; At <70 mg/kg/day effects included dose-related increases in plasma AST, and in some instances increased levels of ALT, with reduced triglyceride and cholesterol levels. Liver weights showed a dose-related decrease as well. The high dose of 69.1 mg/kg/day was associated with histopathological evidence of an effect on the kidney.

Reproductive Toxicity: In female rats, IV doses from 4.3-69.1 mg/kg/day were not associated with any dose-related effects on estrous cycles, mating performance, or pre-implantation losses (excluding the high dose of 69.1 mg/kg/day, where there was a statistically significant increase in pre-implantation loss). In male rats, similar doses were associated with a dose-related increase of blood in the urine. Abnormal sperm morphology, reduced sperm motility and reduced sperm counts were seen in all males at the high dose of 69.1 mg/kg/day, but not at a dose of 17.3 mg/kg/day or lower. Following the recovery period, tubular epithelial atrophy was seen in 3 of 8 high-dose males, and one high-dose male showed reduced sperm motility and abnormal sperm morphology. Tubular epithelial atrophy was seen alone and to a lesser degree at a dose of 17.3 mg/kg/day.

Developmental Toxicity: In rats, IV doses from 4.3-69.1 mg/kg/day were associated with slight reduction in fetal weights and an increased incidence of incomplete ossification. In rabbits, similar effects were seen at doses of 17.3 and 51.8 mg/kg/day and were suggestive of maternal toxicity.

Genotoxicity: Negative in several genotoxicity studies, including the Ames bacterial cell mutagenicity assay, an in vitro chromosomal aberration assay, and an in vivo micronucleus assay in male mice.

Carcinogenicity: No long-term studies in animals have been perform to evaluate the carcinogenic potential of cangrelor. This substance is not listed as a carcinogen by NTP, IARC, ACGIH or OSHA.

Aspiration Hazard: No data available.

Known clinical effects: Cangrelor has been considered to be safe and well-tolerated in human clinical trials. Adverse effects have included platelet, bleeding, and clotting disorders (e.g. prolongation of bleeding time), as well as effects on the gastrointestinal tract. Studies in humans have included treatment for up to 72 hours at a dose of 4 μg/kg/min with no evidence of clinically significant adverse effects on the kidney or urinary tract.

SECTION 12 – ECOLOGICAL INFORMATION

Aquatic Toxicity: No data available

Persistence and Degradability: No data available

Bioaccumulation potential: No data available

Note: The environmental characteristics of the formulated product have not been fully investigated. Releases to the environment should be avoided.

13. Disposal Considerations

Waste treatment methods: Disposal must be according to all applicable regulations.
Do not allow product to reach sewage system.

Contaminated packaging: Disposal must be according to all applicable regulations.

SECTION 14 – TRANSPORT INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION: Not Regulated

IATA: Not Regulated

15. Regulatory Information

Compliance: This SDS complies with the requirements under US, EU and GHS guidelines.

OSHA Hazardous: Yes. May cause blood damage *(e.g.* bleeding).

WHMIS Classification: Not required. Drugs are not subject to WHMIS. This product has been classified in accordance with the hazard criteria of the Controlled Products Regulations and this SDS contains all of the information required by those regulations.

TSCA Status: Not listed.

SARA Section 313: Not listed.

California Proposition 65: Not listed.

16. Other Information

Sources of data: Information from published literature and internal company data.

Abbreviations:
ACGIH - American Conference of Government Industrial Hygienists
ADR/RID European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail;
AIHA -American Industrial Hygiene Association+
CAS# -Chemical Abstract Services Number
DNEL -Derived No Effect Level
DOT - Department of Transportation
EINECS - European Inventory of New and Existing Chemical Substances
ELINCS - European List of Notified Chemical Substances

EU - European Union
GHS -Globally Harmonized System of Classification and Labeling of Chemicals
IARC - International Agency for Research on Cancer
IDLH - Immediately Dangerous to Life or Health
IATA -International Air Transport Association
IMDG - International Maritime Dangerous Goods
LOEL – Lowest Observed Effect Level
LOAEL – Lowest Observed Adverse Effect Level
NIOSII –The National Institute for Occupational Safety and Health;
NOEL -No Observed Effect Level;
NOAEL -No Observed Adverse Effect Level
NTP - National Toxicology Program
OEL –Occupational Exposure Limit
OSHA -Occupational Safety and Health Administration
PNEC –Predicted No Effect Concentration
SARA- Superfund Amendments and Reauthorization Act
STEL –Short Term Exposure limit
TDG - Transport Dangerous Goods
TSCA - Toxic Substances Control Act
TWA - Time Weighted Average
WIIMIS –Workplace Hazardous Materials Information System
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