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Section 1 - Identification


- (a) **Product Identifier:** Bivalirudin RTU Injection
- (b) **Product Code:** 70860-403
- Common/Trade Name:** Bivalirudin RTU Injection
- Chemical Name:** D-phenylalanyl-L-prolyl-L-arginyl-L-prolylglycylglycylglycylglycyl-L-asparagylglycyl-L- α -aspartyl-L-phenylalanyl-L- α -glutamyl-L- α -glutamyl-L-isoleucyl-L-prolyl-L- α -glutamyl-L- α -glutamyl-L-tyrosyl-L-leucine
- Chemical Family:** Anticoagulant Agent
- (c) **Product Use:** Pharmaceutical, Injectable
- Product Type:** Regulated Prescription Drug
- Container Information:** Vial
- (d) **Distributor:** Athenex Pharmaceutical Division, 10 N. Martingale Road, Suite 230, Schaumburg, IL 60173, 847-886-9515
- (e) **Emergency Telephone:** 855-273-0154

Section 2 - Hazards Identification

- (a) **Classification of substance or mixture:**
- NFPA Rating**
 Health Hazard : 2
 Fire Hazard : 0
 Reactivity Hazard : 0

(b) Signal Word, Hazard statement(s), Symbol(s), and/or Precautionary statement(s):

Signal Word:	Danger
Hazard Statement:	Causes severe skin burns and eye damage. Causes serious eye damage. May cause damage to organs through prolonged or repeated exposures
Symbols:	N/A
Precautionary Statements:	N/A
Other Hazards	N/A

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(d) Unknown Acute Toxicity N/A

Section 3 – Composition / Information on Ingredients


(a) Chemical Name	(b) Common Name / Synonym	% Composition or other measure	(c) CAS No.	(d) Impurities / Stabilizing Additives
D-phenylalanyl-L-prolyl-L-arginyl-L-prolyl-glycylglycylglycylglycyl-L-asparagylglycyl-L- α -aspartyl-L-phenylalanyl-L- α -glutamyl-L- α -glutamyl-L-isoleucyl-L-prolyl-L- α -glutamyl-L- α -glutamyl-L-tyrosyl-L-leucine	Bivalirudin trifluoroacetate	5 mg/mL	128270-60-0	N/A
Sodium acetate trihydrate	Acetic acid, sodium salt, trihydrate	0.8 mg/mL	6131-90-4	N/A
Polyethylene glycol 400	PEG 400	100 mg/mL	25322-68-3	N/A
Sodium Hydroxide	Sodium Hydroxide	q.s. to adjust pH to 5.25	1310-73-2	N/A
Glacial acetic acid	Glacial acetic acid	q.s. to adjust pH to 5.25	64-19-7	N/A
Water for Injection	Water for Injection	q.s.	7732-18-5	N/A

q.s. – Quantity Sufficient

Section 4 – First Aid Measures

Eye Exposure: Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Skin Exposure: Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

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Ingestion: Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary

Inhalation: Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Notes to Physician: See patient package insert in shipping carton for complete information

Section 5 – Fire-fighting Measures

- (a) **Extinguishing Media** As with any fire, use extinguishing media appropriate for primary cause of fire such as carbon dioxide, dry chemical extinguishing powder or foam.
- (b) **Hazardous Combustion Products:** None anticipated for this product. Avoid the generation of dusty environments.
- (c) **Special Protective Equipment / Precautions:** No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self-contained breathing apparatus

Section 6 - Accidental Release Measures

Spill: Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Collect powder using techniques that minimize the creation of airborne dust. Clean the area with soap and water. If the spill occurs after reconstitution, absorb the liquid with suitable material and clean affected area with soap and water. Dispose of spill materials according to the applicable federal, state, or local regulations.


Release to Air: N/A

Release to Water: N/A

Section 7 - Handling and Storage

General Handling: Gloves, masks and goggles are recommended during handling.

Storage Conditions: Store at 2° to 8°C (36° to 46°F); excursions permitted between 20° to 25°C (68° to 77°F). Avoid excess heat.

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Section 8 - Exposure Controls / Personal Protection

(a) Exposure Limits


Compound	Issuer	Type	Exposure Limit
Bivalirudin	OSHA ACGIH AIHA	PEL TLV WEEL	NE NE NE (8 hr TWA)
Sodium acetate trihydrate	N/A	N/A	N/A
Polyethylene Glycol 400	AIHA	WEEL	10 (mg/m ³) TWA
Glacial acetic acid	ACGHI	TWA	(25 mg/m ³ TWA) TWA 15 ppm
Sodium hydroxide	OSHA ACGHI AIHA	PEL TLV WEEL	NE (2mg/m ³) NE (2mg/m ³ , Ceiling) NE (8 hr TWA)

(b) Engineering Controls

Engineering controls are normally not needed during the normal use of this product.

(c) Individual Protection Measures


Under normal use and handling conditions, no protective equipment is required. The following is recommended for a production setting.

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Respiratory Protection:	Respiratory protection is normally not needed during intended product use. However, if the generation of dusts or aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N95 or equivalent) is recommended under conditions where airborne dust or aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.
Eye Protection:	Eye protection is normally not required during intended product use. However, if eye contact is likely to occur, the use of chemical safety goggles (as a minimum) is recommended.
Skin Protection:	If skin contact with the product formulation is likely, the use of latex or nitrile gloves is recommended.
Other Protective Equipment:	Not established.
Additional Exposure Precautions:	Not established.

Section 9 - Physical and Chemical Properties

(a)	Appearance	Clear to slightly opalescent, colorless to yellow, sterile solution.
(b)	Odor	Not available
(c)	Odor Threshold	Not available
(d)	pH	5.0 to 5.5
(e)	Melting Point:	Not available
(f)	Initial Boiling Point:	Not available
(g)	Flash Point	Not available
(h)	Evaporation Rate:	Not available
(i)	Flammability	Not available

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(j)	Upper Lower Flammability or Explosion Limits	Not available
(k)	Vapor Pressure:	Not available
(l)	Vapor Density:	Not available
(m)	Relative Density	Not available
(n)	Solubility(ies)	Not applicable
(o)	Partition Coefficient: n-octanol/water	Not available
(p)	Auto-ignition Temperature	Not available
(q)	Decomposition Temperature	Not available
(r)	Viscosity	Not available

Section 10 - Stability and Reactivity

(a)	Reactivity	Not determined
(b)	Chemical Stability	Stable under standard use and storage conditions.
(c)	Possibility of Hazardous Reactions	Not determined.
(d)	Conditions to Avoid	Strong acids and bases, excessive heat.
(e)	Incompatible Materials	Not determined.
(f)	Hazardous Decomposition Products	Not determined. During thermal decomposition, it may be possible to generate irritating vapors

Section 11 - Toxicological Information

(a)	Likely Routes of Exposure	Inhalation, eye/skin contact or ingestion
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(b)	Symptoms related to the physical, chemical and toxicological characteristics	None known from occupational exposure. Inadvertent inhalation of the powder or aerosol (after reconstitution) may produce respiratory irritation, shortness of breath, and coughing. In clinical use, bivalirudin may produce hematological effects (e.g. increased bleeding), cardiovascular effects (potentially fatal thrombosis), and sensitivity-like reactions. In clinical use, nonhemorrhagic adverse effects include back pain, pain (unspecified), nausea, headache, hypotension, injection site pain, insomnia, hypertension, vomiting, pelvic pain, anxiety, bradycardia, dyspepsia, abdominal pain, fever, nervousness, and urinary retention.
(c)	Delayed and immediate effects and chronic effects from short and long-term exposure	None anticipated from normal handling of this product. However, inadvertent skin contact with this product formulation may cause irritation and redness. Sodium hydroxide has produced severe skin irritation in a study in rabbits. Information on the absorption of this product via inhalation or skin contact is not available. Avoid dust or liquid aerosol generation and skin contact.

(d) Acute Toxicity

Component	Type	Route	Species	Dosage
Bivalirudin	LD ₅₀ LD ₅₀	Subcutaneous Subcutaneous	Rat Rabbit	150 mg/kg 150 mg/kg
Sodium acetate trihydrate	LD ₅₀	N/A	N/A	N/A
Polyethylene Glycol 400	LD ₅₀ LD ₅₀	Oral Dermal	Rabbit Rabbit	26800 mg/kg >20000 mg/kg
Mannitol	LD ₅₀	Oral	Rat	13500 mg/kg
Sodium Hydroxide	LD ₅₀	Oral	Rabbit	500 mg/kg

Reproductive Effects: None anticipated from normal handling of this product. Fertility and general reproductive performance in rats were unaffected by subcutaneous doses of bivalirudin up to 150 mg/kg/day. Teratogenicity studies have been performed in rats at subcutaneous doses up to 150 mg/kg/day and rabbits at subcutaneous doses up to 150 mg/kg/day. No evidence of impaired fertility or harm to the fetus attributable to bivalirudin was noted in these studies.

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(e) Hazardous Chemical Listings

NTP: Not Listed IARC: Not Listed OSHA: Carcinogen

Section 12 - Ecological Information

(a) Ecotoxicity	Not determined for product. <ul style="list-style-type: none"> LC50(48hr, flow through) = 189 mg/l in freshwater fish for sodium hydroxide LC50(24hr, static) = 125-160 mg/l in freshwater fish for sodium hydroxide LC50(48hr, static) = 125 mg/l in freshwater fish for sodium hydroxide LC50(96hr static) = 45.4 – 125 mg/l in freshwater fish for sodium hydroxide EC(lethality) = 100 - 156 mg/l in Daphnia for sodium hydroxide
(b) Persistence and degradability	Not determined for product. Bivalirudin is susceptible to bacterial degradation.
(c) Bioaccumulative potential	Not determined for product
(d) Mobility in soil	Not determined for product
(e) Other Adverse Effects	Not determined for product

Section 13 - Disposal Considerations


Waste Disposal: Dispose of any cleanup materials and waste residue according to all applicable laws and regulations.

Container Handling and Disposal: Dispose of container and unused contents in accordance with federal, state and local regulations.

Section 14 - Transport Information

DOT: Not regulated as a dangerous good.
IATA: Not regulated as a dangerous good.
IMDG: Not regulated as a dangerous good.

(a) UN Number	N/A
(b) UN Proper Shipping Name	N/A
(c) Transport Hazard Class(es)	N/A

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(d)	Packing Group	N/A
(e)	Environmental Hazards	N/A
(f)	Transport in bulk (according to Annex II of MARPOL 73/78 and the IBC Code)	N/A
(g)	Special Precautions	N/A

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Athenex Pharmaceutical Division usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

U.S. Regulations:

- TSCA – Not regulated
- CERCLA - Not on this list
- SARA 302 - Not on this list
- SARA 311/312: Not on this list
- SARA 313 - Not on this list
- OSHA – Not on this list

Section 16 - Other Information


As of the date of effectiveness, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:


Athenex Pharmaceutical Division
10 N. Martingale Road, Suite 230
Schaumburg, IL 60173
847-886-9515

Glossary: This glossary contains definitions of general terms used in SDSs. Not all of these Glossary Terms will apply to this SDS.

ACGIH	American Conference of Governmental Industrial Hygienists
AICS	Australian Inventory of Chemical Substances

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AIHA	American Industrial Hygiene Association
ANSI	American National Standards Institute
CAS Number	Chemical Abstract Service Registry Number
CERCLA	Comprehensive Environmental Response Compensation and Liability Act (of
CHAN	Chemical Hazard Alert Notice
CHEMTREC	Chemical Transportation Emergency Center
DOT	Department of Transportation
DSL	Domestic Substances List
ECHA	European Chemicals Agency
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of Notified Chemical Substances
EPA	Environmental Protection Agency
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HEPA	High Efficiency Particulate Air (Filter)
HMIS	Hazardous Materials Identification System
IARC	International Agency for Research on Cancer
ICAO/IATA	International Civil Aviation Organization/International Air Transport
IMO	International Maritime Organization
KOW	Octanol/Water Partition Coefficient
LEL	Lower Explosive Limit
MSDS	Material Safety Data Sheet
MSHA	Mine Safety and Health Administration
NA	Not Applicable, except in Section 14 where NA = North America
NE	Not Established
NADA	New Animal Drug Application
NAIF	No Applicable Information Found
NCI	National Cancer Institute
NDSL	Non-Domestic Substances List
NFPA	National Fire Protection Association
NIOSH	National Institute for Occupational Safety and Health
NPDES	National Pollutant Discharge Elimination System
NOS	Not Otherwise Specified
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
OEL	Occupational Exposure Limit
PEL	Permissible Exposure Limit (OSHA)
RCRA	Resource Conservation and Recovery Act
RQ	Reportable Quantity
RTECS	Registry of Toxic Effects of Chemical Substances
RTU	Ready to Use
SARA	Superfund Amendments and Reauthorization Act
SDS	Safety Data Sheet
STEL	Short Term Exposure Limit
TLV	Threshold Limit Value (ACGIH)
TPQ	Threshold Planning Quantity
TSCA	Toxic Substances Control Act
TWA	Time Weighted Average/8 Hours Unless Otherwise Noted
UEL	Upper Explosive Limit
UN	United Nations

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USP	United States Pharmacopeia
WEEL	Workplace Environmental Exposure Level (AIHA)
WHMIS	Workplace Hazardous Materials Information System

Signature Manifest

Document Number: SDS038

Revision: 01

Title: SDS038-Bivalrudin RTU Injection

All dates and times are in Eastern Standard Time.

SDS Creation

Change Request

Name/Signature	Title	Date	Meaning/Reason
Michael Scribner (MSCRIBNER)	Director of Corporate Quality		
Michael Spengler (MSPENGLER)	QC Applications Specialist		
Christopher Martensen (CMARTENSEN)	Quality Engineer-CSV		
Emily Means (EMEANS)	QA Document Specialist	24 Mar 2020, 10:16:54 AM	Approved

Dept Approval

Name/Signature	Title	Date	Meaning/Reason
John Andre (JANDRE)	Regulatory Affairs Consultant	26 Mar 2020, 01:41:32 PM	Approved

Final QA Approval/Set Effective Date

Name/Signature	Title	Date	Meaning/Reason
Sheila Moran (SMORAN)	VP of Quality Assurance	26 Mar 2020, 01:56:35 PM	Approved