

Safety Data Sheet



Bristol-Myers Squibb Company

1. IDENTIFICATION					
<i>Product Information</i>					
Product name	ELIQUIS® (apixaban)Tablets, 2.5 mg & 5.0 mg				
Version	1.1, 07.03.2013				
Jurisdiction	This Safety Data Sheet was prepared in accordance with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for the United States of America (USA) (CFR 1910.1200), European Union (EU) (EC 1272/2008) and United Nations (UN). The following countries utilize the UN GHS classification process: Mexico, Brazil, China, New Zealand, Canada, Japan, Korea and Australia.				
Active substance	Apixaban				
Synonyms	BMS-562247-01 Tablets; BMS 562247-01 Tablets; AG0023 Tablets; DPH-150123 Tablets				
Other information	Project Name: 020F6				
Intended Uses	This material is a finished drug product for patient use. The primary indication is thrombosis.				
<i>Company/Undertaking Identification</i>					
Address	<table border="0"><tr><td><u>USA</u> Bristol-Myers Squibb Company P.O. Box 191 New Brunswick, New Jersey 08903 United States of America</td><td><u>Ireland</u> Bristol-Myers Squibb Company Swords Laboratories, Watery Lane Swords, Ireland MG-GBS-MSDS-Request@bms.com</td></tr></table>	<u>USA</u> Bristol-Myers Squibb Company P.O. Box 191 New Brunswick, New Jersey 08903 United States of America	<u>Ireland</u> Bristol-Myers Squibb Company Swords Laboratories, Watery Lane Swords, Ireland MG-GBS-MSDS-Request@bms.com		
<u>USA</u> Bristol-Myers Squibb Company P.O. Box 191 New Brunswick, New Jersey 08903 United States of America	<u>Ireland</u> Bristol-Myers Squibb Company Swords Laboratories, Watery Lane Swords, Ireland MG-GBS-MSDS-Request@bms.com				
Emergency Phone Number	<table border="0"><tr><td>USA (also Canada, Puerto Rico and the Virgin Island): 1-800-424-9300</td><td><u>Ireland</u>: 353-1813-9456</td></tr><tr><td colspan="2">Other Countries: See "Section 16" for country-specific emergency phone numbers from CHEMTREC.</td></tr></table>	USA (also Canada, Puerto Rico and the Virgin Island): 1-800-424-9300	<u>Ireland</u> : 353-1813-9456	Other Countries: See "Section 16" for country-specific emergency phone numbers from CHEMTREC.	
USA (also Canada, Puerto Rico and the Virgin Island): 1-800-424-9300	<u>Ireland</u> : 353-1813-9456				
Other Countries: See "Section 16" for country-specific emergency phone numbers from CHEMTREC.					

2. HAZARDS IDENTIFICATION	
Classification and Labelling Common to All Jurisdictions	
Classification	Serious Eye Damage/Eye Irritation - Category 2 Carcinogenicity - Category 2 Specific Target Organ Systemic Toxicity (Single Exposure) - Category 3
Symbol	
Hazard Statements	Causes serious eye irritation. Suspected of causing cancer. (inhalation). May cause respiratory irritation .
Precautionary Statements	Do not breathe dust/fume/gas/mist/vapours/spray. Wash thoroughly after handling. Wear protective gloves/clothing and eye/face protection. Use personal protective equipment as required.

2. HAZARDS IDENTIFICATION	
	Use only outdoors or in a well-ventilated area. Obtain special instructions before use.
Classification and Labelling for Specific Jurisdictions	
USA	
Classification	Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 1
Signal Word	Danger
Hazard Statements	Causes damage to organs (blood, central nervous system, cardiovascular system, eyes) through prolonged or repeated exposure.
Precautionary Statements	Do not eat, drink or smoke when using this product.
EU	
Classification	Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 2
Signal Word	Warning
Hazard Statements	May cause damage to organs (blood, central nervous system, cardiovascular system, eyes) through prolonged or repeated exposure.
UN	
Classification	Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 1
Signal Word	Danger
Hazard Statements	Causes damage to organs (blood, central nervous system, cardiovascular system, eyes) through prolonged or repeated exposure.
Precautionary Statements	Do not eat, drink or smoke when using this product.

3. COMPOSITION/INFORMATION ON INGREDIENTS					
Components	Concentration	CAS-No.	EU only		
			EINECS/ELINCS/REACH Registration Number	Symbol(s)/R-phrases	H-code(s)
<i>Hazardous components</i> Apixaban	2.4 %	Trade Secret	--	T: R48/25	H372
Microcrystalline Cellulose	< 40 %	9004-34-6	232-674-9	Xi: R37	H335

Sodium Lauryl Sulfate	< 1 %	151-21-3	205-788-1	Xn, Xi, N: R21, R22, R36/37/38, R51/53	H302 H311 H315 H318 H335
Magnesium Stearate	< 5 %	557-04-0	209-150-3	--	H372
Hydroxypropyl Methylcellulose	< 5 %	9004-65-3	--	--	H372
Titanium Dioxide	< 1 %	13463-67-7	236-675-5	Xi, Xn: R37, R40, R53	H351 H335 H372 H413
<i>Other ingredients</i>					
Non-Hazardous Ingredients	< 50 %	Not available	--	--	--
See section 16 for Symbol, R-phrases and H-code text.					

4. FIRST AID MEASURES

Eye contact	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical advice/attention.
Skin contact	Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water for at least 15 minutes. If exposed or concerned: Get medical attention/advice.
Inhalation	IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Call a POISON CENTER or doctor/physician if you feel unwell.
Ingestion	Do NOT induce vomiting. Never give anything by mouth to an unconscious person. If exposed or concerned: Get medical attention/advice.
Notes to Physician	This product has been reported to interact with the following medications: drugs that inhibit cytochrome P-450. Refer to Section 11.
Medical Surveillance	A pre-placement physical examination and history for employees with potential exposure to this compound is recommended. Baseline testing would include: a medical history with emphasis on unusual bleeding, a complete blood count with differential. Based on opportunity for exposure and duration of exposure a periodic follow-up examination may be considered. This exam should be overseen by a physician thoroughly knowledgeable about both the toxicity of this compound and the extent of work place exposure. It is recommended that the content be similar to the pre-placement exam. Employees who are pregnant, are breast-feeding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational health physician monitoring worker's health.

5. FIRE-FIGHTING MEASURES

Flammable Properties	Not available
Extinguishing Media	Suitable extinguishing media: Dry chemical, Water spray, Foam Unsuitable extinguishing media: Do NOT use water jet.

5. FIRE-FIGHTING MEASURES

Protection of Firefighters	Specific hazards: Eye irritant Respiratory Irritant Protective equipment: Use personal protective equipment. In the event of fire, wear self-contained breathing apparatus. Hazardous Combustion Products: carbon oxides (COx), nitrogen oxides (NOx), and, sulphur compounds
Other information	Decontaminate protective clothing and equipment before reuse.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions	Refer to protective measures listed in sections 7 and 8. Use personal protective equipment. Examples include tightly fitting safety goggles, lab coat and impervious gloves. Wear respiratory protection. Depending on the nature of the spill (quantity and extent of spill) additional protective clothing and equipment such as a self-contained breathing apparatus may be needed.
Environmental precautions	Prevent release to drains and waterways. Prevent release to the environment.
Containment Methods	Wet down any dust to prevent generation of aerosols, if appropriate. Cover with suitable material.
Cleanup Methods	Contain and collect spillage and place in container for disposal according to local regulations (see Section 13). Handle waste materials, including gloves, protective clothing, contaminated spill cleanup material, etc., as appropriate for chemically and pharmacologically similar materials.

7. HANDLING AND STORAGE

Handling Precautions	Avoid exposure - obtain special instructions before use. Avoid formation of dust and aerosols. When handling broken or crushed tablets or capsules, ensure worker exposure is below the recommended exposure limit. Keep away from heat and sources of ignition. Prevent release to drains and waterways. Use only outdoors or in a well-ventilated area.
Container Requirements	Store in the original primary packaging as provided. Keep container tightly closed.
Storage Conditions	Store at 15-25 °C. Protect against light. Keep away from heat, sparks and flames. Store in well-ventilated place.
Specific use(s)	Refer to Section 1

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Exposure limit(s)	Company Guideline	ACGIH	Germany OEL	UK MEL
Apixaban	3 µg/m ³ 8 hour-TWA	--	--	--
Microcrystalline Cellulose		10 mg/m ³ TWA	--	--
Magnesium Stearate		10 mg/m ³ TWA	--	--
Titanium Dioxide		10 mg/m ³ TWA	--	--

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Red Iron Oxide	5 mg/m3 TWA dust and fume, as Fe 1 mg/m3 TWA as Fe	6 mg/m3 TWA respirable fraction 1.5 mg/m3 MAK respirable fraction	10 mg/m3 STEL fume, as Fe 2 mg/m3 STEL as Fe 5 mg/m3 TWA fume, as Fe 1 mg/m3 TWA as Fe
Microcrystalline Cellulose	Occupational Exposure Limits have been established by: - Belgium - Switzerland - Estonia - Spain - France - Ireland - Portugal		
Magnesium Stearate	Occupational Exposure Limits have been established by: - Belgium - Spain - Ireland - Portugal - Sweden		
Titanium Dioxide	Occupational Exposure Limits have been established by: - Austria - Belgium - Switzerland - Denmark - Estonia - Spain - France - Greece - Ireland - Norway - Poland - Portugal - Sweden		
Red Iron Oxide	Occupational Exposure Limits have been established by: - Austria - Belgium - Switzerland - Czech Republic - Denmark - Estonia - Spain - Finland - France - Greece - Hungary - Ireland - The Netherlands - Norway - Poland - Portugal - Sweden		
Recommended Industrial Hygiene Monitoring Methods	Contact the Bristol-Myers Squibb AIHA accredited Industrial Hygiene Laboratory at 732-227-6338. See Section 4 "Notes to Physician" for information on medical surveillance.		
EXPOSURE CONTROLS / PERSONAL PROTECTION FOR MATERIAL AS SUPPLIED			
<p><u>ELIQUIS® (apixaban) Tablets, 2.5 mg & 5.0 mg</u> 2 -- Material is assigned to Exposure Control Band 2 (range 100 - 1000 µg/m3).</p>			
Engineering Controls and Ventilation	<p>FOR MANUFACTURING PROCESSES (BULK): Use process enclosures, containment technology, or other engineering controls to keep airborne levels below recommended exposure limit. When handling quantities up to 150 milligrams, a standard laboratory with general laboratory dilution ventilation (e.g. 6-12 air changes per hour) is appropriate. When handling quantities from 150 milligrams to 1 kilogram, work in a standard laboratory using a fume hood; biological safety cabinet(Class II, all types), approved vented enclosure; specific local exhaust. Quantities exceeding 1 kilogram should be handled in a designated laboratory. A laminar flow/powder containment booth is recommended for handling >1 kilograms of active substance. For manufacturing and pilot plant operations, use semi to closed material transfer systems and containment of open operations. HEPA filtration for recirculation of exhaust is required.</p> <p>FOR CLINICAL SETTING USE (DRUG PRODUCT): When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed.</p>		

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Respiratory protection	Use and selection of respiratory protection is based upon engineering controls in use and potential for aerosol generation. When engineering controls are not sufficient control exposure, wear an approved respirator with NIOSH Class 100 or high efficiency particulate (HEPA) filters or cartridges (EN 140/EN 136) when exposures are up to 10 times the exposure control guideline. Wear a loose-fitting (Tyvek or helmet type) HEPA powered-air purifying respirator (PAPR) (EN 12941) when exposures are 10-25 times the exposure control guideline. Wear a full facepiece negative pressure respirator with Class 100 or HEPA filters (EN 136) when exposures are 25-50 times the exposure control guideline. Wear a tight-fitting, full facepiece HEPA PAPR (EN 12942) when exposures are 50-100 times the exposure control guideline. Wear a hood-shroud HEPA PAPR (EN 12941) or full facepiece supplied air respirator (EN 139) operated in a pressure demand or other positive pressure mode when exposures are 100-1000 times the exposure control guideline.
Eye protection	Safety glasses with side-shields are recommended (EN 166). Face shields or chemical safety goggles (EN 166) may be required if splash potential exists or if corrosive materials are present. Note: Choice of eye protection may be influenced by the type of respirator which is selected.
Hand protection	Impervious nitrile, rubber and latex gloves are recommended (EN 420, EN 374). If material is handled in solution, the solvent should also be considered when selecting protective clothing material. Please note that employees who are allergic to natural rubber latex should use nitrile gloves.
Skin and body protection	FOR MANUFACTURING PROCESSES (BULK): Wear a laboratory coat (EN 340) when handling quantities up to 1 kilograms. For quantities over 1 kilogram, wear laboratory coat (EN 340) or coverall of low permeability (EN 1149-1). For manufacturing operations, wear coverall of low permeability (EN 1149-1). FOR CLINICAL SETTING USE (DRUG PRODUCT): When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed.
Hygiene	Wash hands and face before breaks and immediately after handling the product.
Environmental exposure controls	Prevent release to drains and waterways.

9. PHYSICAL AND CHEMICAL PROPERTIES

General Information

Appearance

Physical State	solid
Color	yellow pink brown or white to off-white
Form	tablet

Odour

Odour	Not available
Odor Threshold	Not available

pH	Not available
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Other information

Bulk density	Not available
Evaporation rate	Not available
Molecular formula	Not applicable
Hydrolysis/Photolysis	Not available

9. PHYSICAL AND CHEMICAL PROPERTIES

Hygroscopicity	Not available
Molecular Weight	Not applicable
Log Octanol/Water Partition Coeff [log Kow]	Not available
Surface Tension	Not available
pKa	Not available
Particle Size	Not available
Solubility, Water	Not available
Specific Gravity/ Relative density	Not available
Viscosity, dynamic	Not available
Viscosity, kinematic	Not available
% Volatile	Not available
<i>Thermal/Stability properties</i>	
Autoignition temperature	Not available
Boiling Point	Not available
Thermal decomposition	Not available
Explosive Limits, LEL	Not available
Explosive limits, UEL	Not available
Explosiveness	Not available
Flammability	Not available
Flash point	Not available
Melting Point	Not available
Oxidizing Potential	Not available
<i>Vapor Properties</i>	
Vapor Density	Not available
Vapor Pressure	Not available
Saturated Vapor Concentration	Not available

10. STABILITY AND REACTIVITY

Stability

Chemical Stability	Stable under normal conditions.
Conditions to avoid	Not available
Materials to avoid	Not available
Hazardous decomposition products	Hazardous decomposition products formed under fire conditions.: carbon oxides (COx), nitrogen oxides (NOx), and, sulphur compounds
Hazardous reactions	None known.
<i>Sensitivity to static discharge/Dust exp.</i>	
Summary Statements	Although material has not been specifically tested, fine dust suspended in air in sufficient concentration and in the presence of an ignition source may pose a potential explosion hazard. Provide appropriate bonding and grounding protection to control static charge. Powder handling equipment such as dust collectors, dryers, and mills may require additional protective measures (e.g. explosion venting, inerting, etc.).

11. TOXICOLOGICAL INFORMATION

Routes of Entry Ingestion, inhalation, Eye contact, Skin contact

Eye Irritation Apixaban
Not an eye irritant based on in vitro assay

Microcrystalline Cellulose
Mildly irritating to eyes.

Sodium Lauryl Sulfate
Severely irritating to eyes.

Magnesium Stearate
May cause mechanical irritation.

Hydroxypropyl Methylcellulose
Dust may cause mechanical irritation.

Titanium Dioxide
Dust may cause mechanical irritation.

Skin Irritation Apixaban
Not irritating to skin.

Microcrystalline Cellulose
Not irritating to skin.

Sodium Lauryl Sulfate
Irritating to skin.

Magnesium Stearate
May cause mechanical irritation.

Titanium Dioxide
Dust may cause mechanical irritation.

Respiratory
Irritation Microcrystalline Cellulose
Respiratory Irritant

Sodium Lauryl Sulfate
Irritating to respiratory tract.

Titanium Dioxide
Irritating to respiratory tract.

11. TOXICOLOGICAL INFORMATION

Sensitization

Apixaban

Not a dermal sensitizer in an experimental study

Microcrystalline Cellulose

Not a dermal sensitizer

Sodium Lauryl Sulfate

Allergic contact dermatitis is quite rare but has been reported.

Titanium Dioxide

Not a dermal sensitizer

11. TOXICOLOGICAL INFORMATION

Acute Toxicity Study

Acute Oral

Apixaban

LD50 (rat, males and females): > 4,510 mg/kg

LD50 (mouse, males and females): > 4,000 mg/kg

Minimum lethal dose (monkey, males and females): 100 mg/kg Hemorrhaging was considered secondary to inadvertent arterial puncture in association with drug treatment.

LD50 (dog, females): > 1,500 mg/kg No mortality occurred.

Microcrystalline Cellulose

LD50 (rat, males and females): > 5,000 mg/kg

Sodium Lauryl Sulfate

LD50 (rat): 1,288 mg/kg

LD50 (rat): 1,288 mg/kg

LD50 (rat): 1,288 mg/kg

LD50 (rat): 1,288 mg/kg

Titanium Dioxide

LD50 (rat): > 10,000 mg/kg

LD50 (rat): > 10,000 mg/kg

Acute Dermal

Microcrystalline Cellulose

LD50 (rat, males and females): > 2,000 mg/kg

Sodium Lauryl Sulfate

LD50 (rat): > 2,000 mg/kg

LD50 (rabbit): 580 mg/kg

LD50 (rabbit): 580 mg/kg

LD50 (rabbit): 580 mg/kg

LD50 (rabbit): 580 mg/kg

LD50 (guinea pig): 1,200 - 2,000 mg/kg

Titanium Dioxide

LD50 (rabbit): > 10,000 mg/kg

LD50 (rabbit): > 10,000 mg/kg

Acute inhalation toxicity

Microcrystalline Cellulose

LC50 (rat, males and females): > 5350 mg/m³/4 H

Sodium Lauryl Sulfate

LC50 (rat): > 3,900 mg/m³/1hr/1 H

Titanium Dioxide

LC50 (rat): > 2.29 mg/l/4 H/4 H

Acute toxicity (other routes of administration)

Apixaban

LD50 (mouse, males and females, intravenous): 50 mg/kg

Microcrystalline Cellulose

LD50 (rat, males, intraperitoneal): > 3,160 mg/kg

Hydroxypropyl Methylcellulose

LD50 (rat, intraperitoneal): 5,200 mg/kg

LD50 (mouse, intraperitoneal): 5,000 mg/kg

11. TOXICOLOGICAL INFORMATION

Repeated Dose Toxicity Apixaban
12 weeks - 105 weeks oral (daily) mouse, rat, dog study (males and females): NOAEL = 5 mg/kg; Low dose effects include: minimal changes in clinical chemistry parameters, changes in blood clotting parameters. High dose microscopic effects include: lymph nodes. After recovery, all parameters returned to normal.
2 Weeks intravenous (daily) dog study (males and females): NOAEL = 0.4 mg/kg; Low dose effects include: minimal changes in clinical pathology parameters, changes in blood clotting parameters.

Sodium Lauryl Sulfate
2 Years Dietary (daily) rat study : NOAEL = 1%; No significant adverse effects were observed.

Magnesium Stearate
3 months Dietary rat study : NOAEL = 2,500 mg/kg; Low dose effects include: decreased weight gain, liver effects, kidney stones.

Titanium Dioxide
Assessment Repeat Dose Toxicity
Several studies were conducted. See "Human Experience".

Genetic Toxicity Apixaban
In vitro
Ames reverse-mutation assay -- negative
Chromosome aberration test in vitro -- negative
in vivo
3 Days oral, Mutagenicity (micronucleus test) (rat) -- negative
1 months oral, Chromosomal aberrations (rat) -- negative
Mutagenicity Assessment
This material was negative in a battery of in vivo and in vitro genotoxicity assays.

Microcrystalline Cellulose
Mutagenicity Assessment
This material was negative in a battery of in vivo and in vitro genotoxicity assays.

Sodium Lauryl Sulfate
Mutagenicity Assessment
Several studies were conducted. This material was negative in a battery of in vivo and in vitro genotoxicity assays. Not considered a mutagen according to 29 CFR 1910, 67/348/EC or Canadian Controlled Products Regulations.

Titanium Dioxide
Mutagenicity Assessment
This material was negative in a battery of in vivo and in vitro genotoxicity assays.

11. TOXICOLOGICAL INFORMATION

Carcinogenicity Apixaban
104 Weeks Dietary (daily) rat study : Tumor NOAEL = 600 mg/kg (males and females).
No treatment-related tumors were observed.
104 Weeks Dietary (daily) mouse study : Tumor NOAEL = 1,500 mg/kg (males and females). No treatment-related tumors were observed.

Carcinogenicity Assessment

This material did not show carcinogenic potential in animal studies.

Microcrystalline Cellulose

Carcinogenicity Assessment

This material did not show carcinogenic potential in animal studies. Not classifiable as to its carcinogenicity to humans.

Magnesium Stearate

Carcinogenicity Assessment

Not classifiable as to its carcinogenicity to humans.

Titanium Dioxide

Carcinogenicity Assessment

Tumors were observed at high dose in animal studies by inhalation and intratracheal administration. Tumors were not observed by other routes.

Carcinogenicity	ACGIH	IARC	NTP
Apixaban	--	--	--
Microcrystalline Cellulose	--	--	--
Sodium Lauryl Sulfate	--	--	--
Magnesium Stearate	A4	--	--
Hydroxypropyl Methylcellulose	--	--	--
Titanium Dioxide	A4	2B	--

Reproductive Toxicity Apixaban
2 Weeks oral (daily) exposure time = 45 Days Study of Fertility and Early Embryonic Development (rat)
(males and females) LOAEL = 50 mg/kg
Effects include: changes in blood clotting parameters. No effects were found on mating or fertility.

Assessment Reproductive Toxicity

Data indicate that this compound is not a reproductive hazard.

Microcrystalline Cellulose

Assessment Reproductive Toxicity

Data indicate that this compound is not a reproductive hazard.

11. TOXICOLOGICAL INFORMATION

Developmental
Toxicity

Apixaban

10 Days oral (daily) exposure time = 10 Days Study of Embryo-Fetal Development (mouse)
(parent, females) LOAEL = 600 mg/kg
(embryo/fetus) NOAEL = 1500 mg/kg

Maternal effects include: changes in blood clotting parameters. No effects were observed in the fetus/embryo.

9 Days oral (daily) Study of Embryo-Fetal Development (rat)

(parent, females) LOAEL = 100 mg/kg
(embryo/fetus) NOAEL = 3000 mg/kg

Maternal effects include: vaginal discharge, fecal changes. No effects were observed in the fetus/embryo.

12 Days oral (daily) Study of Embryo-Fetal Development (rabbit)

(parent, females) NOAEL = 1500 mg/kg
(embryo/fetus) NOAEL = 1500 mg/kg

No significant adverse effects were observed.

13 Days intravenous (daily) Study of Embryo-Fetal Development (rabbit)

(parent, females) LOAEL = 1.25 mg/kg
(embryo/fetus) NOAEL = 5 mg/kg

Maternal effects include: damage at injection sites, changes in blood clotting parameters. No effects were observed in the fetus/embryo.

oral Study of Pre- and Postnatal Development (rat)

(parent, females) LOAEL = 25 mg/kg
(F1 offspring) NOAEL = 25 mg/kg

Offspring effects include: decreased fertility. Maternal effects include: changes in blood clotting parameters.

Developmental Toxicity Assessment

No adverse developmental effects were observed in animal studies. Anticoagulants may cause increased bleeding during childbirth.

Microcrystalline Cellulose

Developmental Toxicity Assessment

Available data do not indicate a potential for selective developmental toxicity.

Sodium Lauryl Sulfate

Developmental Toxicity Assessment

Adverse effects on the fetus occur only at doses that also cause maternal toxicity.

Human experience

Experiences with Human Exposure

Apixaban

oral Clinical trial(s) low exposure - acute effects include: headache, dizziness, bleeding, bruising, blood in stool, bloody urine, nausea. low exposure - long term exposure effects include: constipation, fever, cerebral bleeding.

Titanium Dioxide

Incident report(s) worker exposure low exposure - acute effects include: cough, breathing difficulties, rhinitis, Irritating to respiratory system..

11. TOXICOLOGICAL INFORMATION

Target Organs	<u>Apixaban</u> blood <u>Magnesium Stearate</u> central nervous system, cardiovascular system <u>Hydroxypropyl Methylcellulose</u> Eyes <u>Titanium Dioxide</u> lungs
Symptoms	<u>Apixaban</u> See "Human Experience". <u>Microcrystalline Cellulose</u> labored respiration, noisy respiration, chest pain, breathing difficulties, shortness of breath, lung inflammation <u>Sodium Lauryl Sulfate</u> nausea, vomiting, diarrhoea, dryness and cracking of skin, rash, redness and swelling of skin and eyes, breathing difficulties, cough, chest pain, congestion, burning, laryngitis <u>Magnesium Stearate</u> redness and swelling of eyes, skin flushing, nausea, vomiting, diarrhoea, dehydration, lowered blood pressure, cardiac irregularities, CNS depression, respiratory disorder, paralysis
Pharmacokinetics/ Toxicokinetics	<u>Apixaban</u> Absorption: Not available Distribution: Not available Metabolism: Not available Elimination: Half-life = 12 Hour(s) (Human).
Other Toxicity Information	Other Toxicity Tests <u>Apixaban</u> Telemetry Study (dog) : intravenous = 1.25 - 4 mg/kg No significant adverse effects were observed. No significant cardiovascular or hemodynamic effects noted. Phototoxicity : In vitro = negative

12. ECOLOGICAL INFORMATION

Ecotoxicity effects

Acute Toxicity to Fish

Sodium Lauryl Sulfate

LC50 (Pimephales promelas (fathead minnow), 96 H) : 10.2 mg/l.

LC50 (Oncorhynchus mykiss (rainbow trout), 96 H) : 4.6 mg/l.

Acute Toxicity to Aquatic Invertebrates

Sodium Lauryl Sulfate

EC50 (Daphnia, 48 H) : 1.8 mg/l.

Toxicity to aquatic plants

Apixaban

EC50 (Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum)) : > 23 mg/l

NOEC (Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum)) : 3.6 mg/l

Sodium Lauryl Sulfate

EC50 (Scenedesmus subspicatus, 72 H) : 53 mg/l

Toxicity to microorganisms

Apixaban

Respiration inhibition, EC50 : > 1,000 mg/l

Sodium Lauryl Sulfate

EC50 (Photobacterium phosphoreum, 5 Minute) : 1.19 mg/l

Chronic toxicity to fish

Apixaban

Early-life Stage LOEC (Pimephales promelas (fathead minnow)) : > 10 mg/l NOEC : 10 mg/l

Chronic toxicity to aquatic invertebrates

Apixaban

LOEC (Daphnia magna (Water flea)) : 23 mg/l

NOEC (Daphnia magna (Water flea)) : 9.6 mg/l

Mobility Not available

Persistence and degradability

Biodegradation

Apixaban

Ready biodegradation : 0 % ; Not readily biodegradable.

Apixaban

Koc (soil) : 12.2

PBT and vPvB Assessment: Not available

13. DISPOSAL CONSIDERATIONS

Advice On Disposal And Packaging

Disposal should be in accordance with applicable regional, national and local laws and regulations. Local regulations may be more stringent than regional or national requirements. This information presented only applies to the material as supplied.

Other information

This information presented only applies to the material as supplied.

14. TRANSPORT INFORMATION

This material is not a dangerous good for the purpose of transportation.

15. REGULATORY INFORMATION

United States of America

15. REGULATORY INFORMATION

313 Toxic Release Inventory No components listed on the SARA 313 inventory.

TSCA Inventory Not listed. Food, drug and cosmetic products are exempt from TSCA.

EU Directive 1999/45/EC

BULK MATERIAL

Symbol(s) Xn: Harmful
Xi: Irritant

R-phrases R37: Irritating to respiratory system.
R40: Limited evidence of a carcinogenic effect.
inhalation
R48/22: Harmful: danger of serious damage to health by prolonged exposure if swallowed.

S-phrases S22: Do not breathe dust.
S36/37/39: Wear suitable protective clothing, gloves and eye/face protection.
S38: In case of insufficient ventilation, wear suitable respiratory equipment.
S45: In case of accident or if you feel unwell, seek medical advice immediately (show label where possible).
S53: Avoid exposure - obtain special instructions before use.
S60: This material and its container must be disposed of as hazardous waste.

DRUG PRODUCT

Classification Medicinal products are exempt from classification and labeling requirements under EU Preparations Directive 1999/45/EC.

Regulatory Authorizations and Restrictions: Not available

16. OTHER INFORMATION

Text of Symbol(s), R-phrases(s) and H-code(s) mentioned in Section 3

H302	Harmful if swallowed.
H311	Toxic in contact with skin.
H315	Causes skin irritation.
H318	Causes severe eye damage.
H335	May cause respiratory irritation
H351	Suspected of causing cancer.
H372	Causes damage to organs through prolonged or repeated exposure.
H413	May cause long lasting harmful effects to aquatic life.
N	Dangerous for the environment
R21	Harmful in contact with skin.
R22	Harmful if swallowed.
R36/37/38	Irritating to eyes, respiratory system and skin.
R37	Irritating to respiratory system.
R40	Limited evidence of a carcinogenic effect.
R48/25	Toxic: danger of serious damage to health by prolonged exposure if swallowed.
R51/53	Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

R53 May cause long-term adverse effects in the aquatic environment.
 T Toxic
 Xi Irritant
 Xn Harmful

Recommended Restrictions for Use:

Not available

SDS preparation information

Prepared by Research and Development Environment, Health and Safety 1-732-227-7380

Prepared on 07.03.2013 DD/MM/YYYY

This Safety Data Sheet has been revised. This data sheet contains changes from the previous version in section(s): 1, and 16.

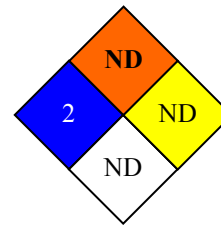
Other information

HMIS

Health	2*
Flammability	Not Determined (ND)
Reactivity	Not Determined (ND)
Personal protective equipment	See Section 8.

NFPA

Health 2
 Fire ND
 Reactivity ND
 Special ND



Country- Specific Emergency Phone Numbers

CHEMTREC In-Country Dial Numbers	Local # Provided in Country	Toll Free in Country*	Greeting Language
CHEMTREC South Africa*		0-800-983-611	English
CHEMTREC Argentina (Buenos Aires)	+(54)-1159839431		Latin American Spanish
CHEMTREC Brazil (Rio De Janeiro)	+(55)-2139581449		Portuguese
CHEMTREC Chile (Santiago)	+(56)-25814934		Latin American Spanish
CHEMTREC Colombia *		01800-710-2151	Latin American Spanish
CHEMTREC Mexico*		01-800-681-9531	Latin American Spanish
CHEMTREC Peru (Lima)	+(51)-17071295		Latin American Spanish
CHEMTREC China*	4001-204937		Mandarin
CHEMTREC Hong Kong (Hong Kong)*		800-968-793	Cantonese
CHEMTREC India *		000-800-100-7141	Hindi
CHEMTREC Indonesia *		001-803-017-9114	Indonesian
CHEMTREC Japan (Tokyo)	+(81)-345209637		Japanese
CHEMTREC Malaysia *		1-800-815-308	Malay
CHEMTREC Philippines *		1-800-1-116-1020	Tagalog
CHEMTREC Singapore*		800-101-2201	Mandarin
CHEMTREC Singapore	+(65)-31581349		Mandarin
CHEMTREC South Korea*		00-308-13-2549	Korean
CHEMTREC Taiwan*		00801-14-8954	Mandarin
CHEMTREC Thailand *		001-800-13-203-9987	Thai
CHEMTREC Vietnam (Ho Chi Minh City)	+(84)-838012436		Vietnamese
CHEMTREC Australia (Sydney)	+(61)-290372994		English
CHEMTREC Belgium (Brussels)	+(32)-28083237		French and Flemish
CHEMTREC Czech Republic (Prague)	+(420)-228880039		Czech
CHEMTREC France	+(33)-975181407		French
CHEMTREC Germany *		0800-181-7059	German
CHEMTREC Hungary (Budapest)	+(36)-18088425		Hungarian
CHEMTREC Italy *		800-789-767	Italian
CHEMTREC Italy (Milan)	+(39)-0245557031		Italian
CHEMTREC Netherlands	+(31)-858880596		Dutch
CHEMTREC Poland (Warsaw)	+(48)-223988029		Polish
CHEMTREC Spain*		900-868538	European Spanish
CHEMTREC Sweden (Stockholm)	+(46)-852503403		Swedish
CHEMTREC Switzerland (Zurich)	+(41)-435016715		German
CHEMTREC UK (London)	+(44)-870-8200418		English
CHEMTREC Bahrain (Bahrain)	+(973)-16199372		Arabic
CHEMTREC Israel (Tel Aviv)	+(972)-37630639		Hebrew
*Phone numbers for countries marked with an asterisk must be dialed within the country			

The information contained in this SDS is believed to be accurate and represents the best information reasonably available at the time of preparation. However, we make no warranty, express or implied, with respect to such information. and we assume no liability from its use.