Safety Data Sheet

Bristol Myers Squibb™

1. IDENTIFICATION	
Product Information	
Product name	Mavacamten
Version	2.0, 17.11.2021
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).
Chemical Name	Trade Secret
Synonyms	MYK-461; BMS-986427-01; BMS 986427-01; FP0091; PH-MKD-010; SAR439152; 6-[[(1S)-1-phenylethyl]amino]-3-propan-2-yl-1Hpyrimidine-2,4-dione
Other information	Project Name: 99A28
Intended Uses	This material is used for Research and Development activities. This material is the active pharmaceutical ingredient (API) in a drug product. It is under investigation for the treatment of hypertrophic cardiomyopathy.
Company/Undertaking Identification	
Address	**Bristol-Myers Squibb Company** E-mail: MG-GBS-MSDS-Request@bms.com P.O. Box 191 New Brunswick, New Jersey 08903 United States of America 1-800-332-2056
Emergency Phone Number	CHEMTREC 1-800-424-9300. For all international transportation emergencies call CHEMTREC at 1-703-527-3887. Collect calls accepted.

2. HAZARDS IDENTIFICATION	
Classification and labelling	
Classification	Toxic To Reproduction - Developmental Toxicity - Category 1B Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 1 Substance not fully tested.
Symbol	
Signal Word	Danger
Hazard Statements	May damage the unborn child (developmental toxicity) . Causes damage to organs (cardiovascular system) through prolonged or repeated exposure.
Precautionary Statements	Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Use personal protective equipment as required.

2. HAZARDS IDENTIFICATION

	Do not breathe dust. Wash thoroughly after handling. Do not eat, drink or smoke when using this product.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Components	Concentration	CAS No.	H-code(s)
Hazardous components Mavacamten	100 %	1642288-47-8	H360D H372

See section 16 for H-code text.

4. FIRST AID MEASURES

Eye contact	Rinse immediately with plenty of water for at least 15 minutes. Keep eye wide open while rinsing. If exposed or concerned: Get medical attention/advice.
Skin contact	Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water for at least 15 minutes. Discard contaminated clothing or wash before re-use. If exposed or concerned: Get medical attention/advice.
Inhalation	Move to fresh air. Oxygen or artificial respiration if needed. If exposed or concerned: Get medical attention/advice.
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	Material not fully tested. Refer to Section 11.
Medical Surveillance	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.
Protection of Firefighters	Specific hazards: Not available 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)
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, disposable lab coat of low permeability with cuffs, double gloves and shoe covers. 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	Spill prevention procedures and a spill response procedure should be implemented. Contain and collect spillage and place in container for disposal according to local regulations (see Section 13). Clean spill area with a deactivating solution (if available) followed by detergent and water after spill pick-up. 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	Highly potent material. Avoid exposure - obtain special instructions before use. Avoid formation of dust and aerosols. Keep away from heat and sources of ignition. Prevent release to drains and waterways.
Container Requirements	Store in sturdy containers appropriate to maintain the integrity of this material for its intended use.
Storage Conditions	Store at room temperature. Protect against light. Store preferably under anhydrous conditions. Keep away from heat, sparks and flames. Avoid temperature extremes. Store locked up.
Specific use(s)	Refer to Section 1

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Exposure limit(s)	Company Guideline	ACGIH	Germany OEL	UK MEL
Mavacamten	3 µg/m3	--	--	--

Recommended Industrial Hygiene Monitoring Methods	A specific exposure sampling method is not available. General - The health hazard risk of handling this material is dependent on many factors, including physical form, % of hazardous component(s), hazards associated with other ingredients (e.g. solvents), duration and frequency of process task, and effectiveness of controls. If it is necessary to handle this compound outside of engineering controls, an exposure risk assessment should be conducted and procedures documented by an qualified EHS professional.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION	
Engineering Controls and Ventilation	When handling quantities up to 3 milligrams, a standard laboratory with general laboratory dilution ventilation (e.g. 6-12 air changes per hour) is appropriate. When handling quantities up to > 3 milligrams - 100 grams work in a standard laboratory using approved exposure control device including ventilated balance safety enclosure, Biosafety Cabinets (Type II, all), and Chemical Fume Hood. When handling quantities up to >100 grams - 500 grams, work in either a standard laboratory or designated laboratory (based on unit operations that may increase exposure), using approved exposure control device including ventilated balance safety enclosure, Biosafety Cabinets (Type II, all), and Chemical Fume Hood. When handling quantities up to >500 grams - 1 kilogram, work in a designated laboratory using approved exposure control device including ventilated balance safety enclosure, Biosafety Cabinets (Type II, all), and Chemical Fume Hood. When working with quantities >20 grams - 1 kilogram, fully enclosed process in place of required engineering controls is an acceptable substitution. For Internal laboratory use only: A documented risk assessment is required. when handling quantities exceeding the maximum amount noted. For manufacturing and pilot plant operations, barrier/containment technology and direct coupling (totally enclosed processes that create a barrier between the equipment and the room) with use of double or split butterfly valves, hybrid unidirectional airflow/local exhaust ventilation solutions (e.g. powder containment booth) should be used. Glove bags, isolator/glove box systems are optional.
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	Wear gloves at all times when handling containers, including when unpacking, inspecting or transporting within a facility. Impervious gloves are recommended. (EN 420, EN 374). Double gloving for all manufacturing personnel potentially in direct contact with the compound should be considered. If material is handled in solution, the solvent should also be considered when selecting protective clothing material.
Skin and body protection	Wear a standard or disposable laboratory coat (EN 340) or coverall when handling quantities up to 100 grams. Wear a disposable laboratory coat (EN 340) or coverall when handling quantities >100 grams.. For manufacturing operations, wear disposable coverall of low permeability (EN 1149-1) and disposable shoe covers.
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	white to off-white
Form	crystalline powder

Odour

Odour	Not available
Odor Threshold	Not available

Important health safety and environmental information

pH	Not available

Other information

Bulk density	Not available
Chemical Name	Trade Secret
Evaporation rate	Not available
Molecular formula	C15 H19 N3 O2
Hydrolysis/Photolysis	Not available
Hygroscopicity	Not available
Molecular Weight	273.3 g/mol
Log Octanol/Water Partition Coefficient [log Kow]	2.09
Surface Tension	Not available
pKa	Not available
Particle Size	Not available
Solubility, Water	0.02 g/l (practically insoluble)
Solubility in other solvents	Buffer solution: (as aqueous solution), practically insoluble methanol: sparingly soluble ethyl alcohol: sparingly soluble dimethyl sulfoxide: freely soluble N-methylpyrrolidinone: freely soluble
Specific Gravity/ Relative density	Not available
Viscosity, dynamic	Not available
Viscosity, kinematic	Not available
% Volatile	Not available

Thermal/Stability properties

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	240 °C
Oxidizing Potential	Not available

Vapor Properties

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)
Hazardous reactions	None known.
Sensitivity to static discharge/Dust exp.	
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	Not available
Skin Irritation	Not available
Respiratory Irritation	Not available
Sensitization	Not available
Acute Toxicity Study	**Acute Oral** Maximum tolerated dose (MTD) (dog): < 30 mg/kg low exposure effects include (<= 300 mg/kg): mortality.
Repeated Dose Toxicity	6 weeks - 9 months oral (daily) rat, dog study with recovery period (1 month - 3 months) (males and females): NOAEL (9 months, dog) = 0.06 mg/kg; Low dose effects include (< = 100 mg/kg): clinical signs, decreased body weight, decreased food consumption, heart failure, echocardiographic changes, changes in ECG parameters, increase in heart rate, changes in clinical chemistry parameters, increased organ weights included:, heart, moribundity, mortality. Low dose microscopic effects include: heart, liver, lungs, pancreas, lymph nodes, thymus. Effects still present after recovery include: increased organ weights included:, heart. Microscopic changes were observed in the following organs: heart
Genetic Toxicity	**In vitro** Ames reverse-mutation assay -- negative Micronucleus assay (screening) -- negative **in vivo**

11. TOXICOLOGICAL INFORMATION

2 Days oral, micronucleus assay (rat) -- negative

Mutagenicity Assessment

This material was positive in a battery of in vivo and in vitro genotoxicity assays.

Carcinogenicity

2 Years oral (daily) rat study : Tumor NOAEL = 0.6 mg/kg (males and females). No treatment-related tumors were observed.

6 months oral (daily) mouse study : Tumor NOAEL = 2 mg/kg (males and females). No treatment-related tumors were observed.

Carcinogenicity Assessment

This material did not show carcinogenic potential in animal studies.

Carcinogenicity	ACGIH	IARC	NTP
Mavacamten	--	--	--

Reproductive Toxicity

oral (daily) Study of Fertility and Early Embryonic Development (rat)
(parent, males) NOAEL = 1.2 mg/kg
(parent, females) NOAEL = 1.2 mg/kg
No effects were found on mating or fertility. No effects were observed in the fetus/embryo.

oral (daily) Multi-Generation Study (rat)
(embryo/fetus) NOAEL = 1.5 mg/kg
(F1 offspring) NOAEL = 1.5 mg/kg
This substance did not cause adverse effects on male or female reproduction or on the offspring of treated animals.

Assessment Reproductive Toxicity

Data indicate that this compound is not a reproductive hazard.

Developmental Toxicity

12 Days oral (daily) Study of Embryo-Fetal Development (rat)
(parent, females) NOAEL = 1.5 mg/kg
(embryo/fetus) NOAEL = 0.75 mg/kg
Fetal effects include: postimplantation loss, decreased body weight, malformations. Substance was harmful to the fetus at doses that did not produce adverse effects in the maternal animal.

14 Days oral (daily) Study of Embryo-Fetal Development (rabbit)
(parent, females) NOAEL = 0.6 mg/kg
(embryo/fetus) NOAEL = 0.6 mg/kg
Fetal effects include: malformations. Maternal effects include: decreased body weight, decreased weight gain, decreased food consumption, mortality. Teratogenic effects occur only at doses which also produce adverse effects in the maternal animal.

Developmental Toxicity Assessment

Selective developmental toxicant

Human experience

Experiences with Human Exposure

oral Clinical trials – healthy volunteers, patient population
exposure time = 1 day - 2 years (1x/day - 2x/day) low exposure - acute effects include: irregular heart rate, cardiac arrest, decreased ejection fraction, lightheadedness, hypotension, diarrhea, nausea, vomiting, fatigue, dizziness, headache, hypoactivity.

11. TOXICOLOGICAL INFORMATION

Target Organs	cardiovascular system
Symptoms	See "Human Experience".
Pharmacokinetics/ Toxicokinetics	Absorption: Data available upon request. Distribution: Data available upon request. Metabolism: Data available upon request. Elimination: Half-life = 6 - 23 Day(s) (Human).
Other Toxicity Information	**Other Toxicity Tests** Telemetry Study (dog) : oral = decrease in blood pressure increase in heart rate changes in ECG parameters increased respiration decreased tidal volume Cardiovascular changes were observed. Respiratory changes were observed.

12. ECOLOGICAL INFORMATION

Ecotoxicity effects	Not available
Mobility	Not available
Persistence and degradability	Not available
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	Disposal by incineration is recommended.

14. TRANSPORT INFORMATION

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

15. REGULATORY INFORMATION

United States of America

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.
Regulatory Authorizations and Restrictions:	Not available

16. OTHER INFORMATION		
Text of H-code(s) mentioned in Section 3.		
	H360D	May damage the unborn child
	H372	Causes damage to organs through prolonged or repeated exposure.
Recommended Restrictions for Use:		
	Not available	
SDS preparation information		
Prepared by	Global Environment, Health, Safety, and Sustainability 1-732-227-7380	
Prepared on	17.11.2021 DD/MM/YYYY	
	This Safety Data Sheet has been revised. This data sheet contains changes from the previous version in section(s): 8, 9, 11, and 16. This Safety Data Sheet was prepared for the United States of America (USA).	

Country- Specific Emergency Phone Numbers

Country	Local # or Toll Free in Country*	Greeting Language	Country	Local # or Toll Free in Country*	Greeting Language
AMERICAS			Latvia (Riga)	+(371)-66165504	Latvian
Argentina (Buenos Aires)	+(54)-1159839431	Latin American Spanish	Lithuania (Vilnius)	+(370)-52140238	Lithuanian
Brazil (Rio De Janeiro)	+(55)-2139581449	Portuguese	Luxembourg	+(352)-20202416	French, German, Luxembourgish
Cayman Islands	+(1)-345-749-8392	English	Netherlands	+(31)-858880596	Dutch
Chile (Santiago)	+(56)-225814934	Latin American Spanish	Norway (Oslo)	+(47)-21930678	Norwegian
Colombia *	01800-710-2151	Latin American Spanish	Poland (Warsaw)	+(48)-223988029	Polish
Costa Rica*	+(506)-40003869	Latin American Spanish	Portugal	+(351)-308801773	Portuguese
Mexico*	01-800-681-9531	Latin American Spanish	Romania	(+40)-37-6300026	Romanian
Panama	+(507)-8322475	Latin American Spanish	Russia*	8-800-100-6346	Russian
Peru (Lima)	+(51)-17071295	Latin American Spanish	Slovakia (Bratislava)	+(421)-233057972	Slovak
Trinidad and Tobago*	+(1)-868-224-5716	English	Slovenia (Ljubljana)	+(386)-18888016	Slovene/Slovenian
EUROPE			Spain (Barcelona)	+(34)-931768545	European Spanish
			Spain*	900-868538	European Spanish
Austria (Vienna)	+(43)-13649237	German	Sweden (Stockholm)	+(46)-852503403	Swedish
Belgium (Brussels)	+(32)-28083237	French, Flemish, German	Switzerland (Zurich)	+(41)-435082011	Swiss German, French and Italian
Bulgaria (Plovdiv)	+(359)-32570104	Bulgarian	Turkey (Istanbul)	+(90)-212-7055340	Turkish
Croatia (Zagreb)	+(385)-17776920	Croatian	Ukraine	+(380)-947101374	Ukrainian
Czech Republic (Prague)	+(420)-228880039	Czech	UK (London)	+(44)-870-8200418	English
Finland (Helsinki)	+(358)-942419014	Finnish	**EAST ASIA**		
France	+(33)-975181407	French	China	86-21-33235036	Mandarin
Germany *	0800-181-7059	German	Hong Kong*	800-968-793	Cantonese
Denmark	+(45)-69918573	Danish	Japan	+(81)-345209637	Japanese
Estonia	+(372-6681294	Estonian	Singapore	+(65)-31581349	English and Mandarin
Germany (Frankfurt)	+(49)-69643508409	German	South Korea	+(82) 070-7686-0086	Korean
Greece (Athens)	+(30)-2111768478	Greek	**AUSTRALIA & OCEANIA**		
Hungary (Budapest)	+(36)-18088425	Hungarian	Australia (Sydney)	+(61)-290372994	English
Italy *	800-789-767	Italian	New Zealand*	+(64)-98010034	English
Italy (Milan)	+(39)-245557031	Italian	India *	000-800-100-7141	Hindi

*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.