Merck Animal Health
One Merck Dr.
Whitehouse Station, NJ 08889

MATERIAL SAFETY DATA SHEET

Merck Animal Health urges each user or recipient of this MSDS to read the entire data sheet to become aware of the hazards associated with this material.

SECTION 1. IDENTIFICATION OF SUBSTANCE AND CONTACT INFORMATION

MSDS NAME: **13.64% w/w CBPI Flavored Chewable Tablet for Dogs**

SYNONYM(S): 13.64% w/w CBPI Flavored Chewable Tablet for Dogs
BRAVECTO

MSDS NUMBER: SP002574

EMERGENCY NUMBER(S): Rocky Mountain Poison Center (For Human Exposure):
(303) 595-4869

Animal Health Technical Services:
For Animal Adverse Events: Small Animals and Horses: (800) 224-5318
For Animal Adverse Events: Livestock: (800) 211-3573
For Animal Adverse Events: Poultry: (800) 219-9286

(908) 423-6000 (24/7/365) English Only
Emergencies - CHEMTREC:
(800) 424-9300 (Inside Continental USA)
(703) 527-3887 (Outside Continental USA)

INFORMATION: Animal Health Technical Services:
For Small Animals and Horses: (800) 224-5318
For Livestock: (800) 211-3573
For Poultry: (800) 219-9286

MERCK MSDS HELPLINE: (800) 770-8878 (US and Canada)
(908) 473-3371 (Worldwide)
Monday to Friday, 9am to 5pm (US Eastern Time)

SECTION 2. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

Chewable tablet
Light to dark brown
Odor unknown
May cause allergic reactions in susceptible individuals.
May cause effects to:
gastrointestinal tract
cardiovascular system
respiratory system
kidney
liver
Very toxic to aquatic organisms.

POTENTIAL HEALTH EFFECTS:

SECTION 2. HAZARDS IDENTIFICATION

The toxicological properties of the mixture(s) have not been fully characterized in humans or animals. Therefore, laboratory or process control systems and appropriate work practices should be in place to minimize the potential for inhalation exposure, skin contact, eye contact, or ingestion when working with this material. The information presented below pertains to the following individual ingredients, and not to the mixture(s).

CBPI produced reversible metabolic liver effects in oral and dermal animal studies including increased liver enzyme activity in blood plasma with decreased lipid and protein concentration, increased organ weight, and increased hepatocellular fatty change.

Acute exposure to polyethelyene glycol may cause slight eye or skin irritation, abnormal taste, gas, nausea, vomiting, diarrhea, irregular heartbeat, low blood pressure, or fluid in the lungs. Repeated exposure of polyethylene glycol to damaged skin has been reported to cause kidney failure and necrosis. It may cause skin sensitization in sensitive individuals. Allergic skin reactions have been reported following ingestion of polyethylene glycol.

LISTED CARCINOGENS

No carcinogens or potential carcinogens listed by OSHA, IARC, NTP or ACGIH are present in concentrations >0.1% in this mixture.

SECTION 3. COMPOSITION AND INFORMATION ON INGREDIENTS

CHEMICAL NAME: 4-[5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4H-isoxazol-3-yl]-2-methyl-N-[2-oxo-2-(2,2,2-trifluoroethylamino)ethyl]benzamide-
(CBPI: Active Pharmaceutical Ingredient)

CHEMICAL FAMILY: Isoxazoline derivative in formulation

PRODUCT USE: Veterinary product

CHEMICAL FORMULA: C22 H17 Cl2 F6 N3 O3
(CBPI: Active Pharmaceutical ingredient)

MOLECULAR WEIGHT: 556.3 (CBPI: Active Pharmaceutical Ingredient)

The formulation for this product is proprietary information. Only hazardous ingredients in concentrations of 1% or greater and/or carcinogenic ingredients in concentrations of 0.1% or greater are listed in the Chemical Composition table. Active ingredients in any concentration are listed. For additional information about carcinogenic ingredients see Section 2.

CHEMICAL COMPOSITION

INGREDIENT	CAS NUMBER	PERCENT
Fluralaner (CBPI)	864731-61-3	13.64
Starch	9005-25-8	10 - 20
Polyethylene Glycol	25322-68-3	10 - 20
Sucrose	57-50-1	<10
Glycerin	56-81-5	<10

ADDITIONAL INFORMATION: This MSDS is written to provide health and safety information for individuals who will be handling the final product formulation during research, manufacturing, and distribution. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate MSDS for each ingredient. Refer to the package insert or product label for handling guidance for the consumer.

SECTION 4. FIRST AID MEASURES

INHALATION: Remove to fresh air. If any trouble breathing, get immediate medical attention. Administer artificial respiration if breathing has ceased. If irritation or symptoms occur or persist, consult a physician.

SKIN CONTACT: In case of skin contact, while wearing protective gloves, carefully remove any contaminated clothing, including shoes, and wash skin thoroughly with soap and water. If irritation or symptoms occur or persist, consult a physician.

EYE CONTACT: In case of eye contact, immediately rinse eyes thoroughly with plenty of water. If wearing contact lenses, remove only after initial rinse, and continue rinsing eyes for at least 15 minutes. If irritation occurs or persists, consult a physician.

INGESTION: Rinse mouth and drink a glass of water. Do not induce vomiting unless under the direction of a qualified medical professional or Poison Control Center. If symptoms persist, consult a physician.

SECTION 5. FIRE FIGHTING MEASURES

FLAMMABILITY DATA:

Flash Point: Not determined (liquids) or not applicable (solids).

SPECIAL FIRE FIGHTING PROCEDURES:
Wear full protective clothing and self-contained breathing apparatus (SCBA).

SUITABLE EXTINGUISHING MEDIA:
Carbon dioxide (CO2), extinguishing powder or water spray.

See Section 9 for Physical and Chemical Properties.

SECTION 6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS:
Wear appropriate personal protective equipment as specified in Section 8. Keep personnel away from the clean-up area.

SPILL RESPONSE / CLEANUP:
All spills should be handled according to site requirements and based on precautions cited in the MSDS. In the case of liquids, use proper absorbent materials. For laboratories and small-scale operations, incidental spills within a hood or enclosure should be cleaned by using a HEPA filtered vacuum or wet cleaning methods as appropriate. For large dry or liquid spills or those spills outside enclosure or hood, appropriate emergency response personnel should be notified. In manufacturing and large-scale operations, HEPA vacuuming prior to wet mopping or cleaning is required.

ENVIRONMENTAL PRECAUTIONS:
This product is very toxic to aquatic organisms. Do not allow product to reach ground water, water course, sewage or drainage systems.

See Sections 9 and 10 for additional physical, chemical, and hazard information.

SECTION 7. HANDLING AND STORAGE

HANDLING:
Keep containers adequately sealed during material transfer, transport, or when not in use. Wash face, hands, and any exposed skin after handling. Do not eat, drink, or smoke when using this substance or mixture.

Appropriate handling of this material is dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. See Section 8 (Exposure Controls) for additional guidance.

STORAGE:
Store in a cool, dry, well ventilated area.

See Section 8 for exposure controls and additional safe handling information.

SECTION 8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

EXPOSURE CONTROLS
The health hazard risks of handling this material are dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. Exposure controls for normal operating or routine procedures follow a tiered strategy. Engineering controls are the preferred means of long-term or permanent exposure control. If engineering controls are not feasible, appropriate use of personal protective equipment (PPE) may be considered as alternative control measures. Exposure controls for non-routine operations must be evaluated and addressed as part of the site-specific risk assessment.

RECOMMENDED PERSONAL PROTECTIVE EQUIPMENT (PPE):

Respiratory Protection: Respiratory protective equipment (RPE) may be required for certain laboratory and large-scale manufacturing tasks if potential airborne breathing zone concentrations of substances exceed the relevant exposure limit(s). Workplace risk assessment should be completed before specifying and implementing RPE usage. Potential exposure points and pathways, task duration and frequency, potential employee contact with the substance, and the ability of the substance to be rendered airborne during specific tasks should be evaluated. Initial and ongoing strategies of quantitative exposure measurement should be obtained as required by the workplace risk assessment. All RPE must conform to local and regional specifications for efficacy and performance. Consult your site or corporate health and safety professional for additional guidance.

Skin Protection: Gloves that provide an appropriate barrier to the skin are recommended if there is potential for contact with this material. Consult your site safety staff for guidance.

Eye Protection: Safety glasses with side shields. Use of goggles or full face protection may be required based on hazard, potential for contact, or level of exposure. Consult your site safety staff for guidance.

Body Protection: In small-scale or laboratory operations, lab coats or equivalent protection is required. Disposable Tyvek or other dust impermeable suit should be considered based on procedure or level of exposure. Use of additional PPE such as shoe coverings, gauntlets, hood, or head covering may be necessary. Consult your site safety staff for guidance.

In large-scale or manufacturing operations, disposable Tyvek or other dust impermeable suit is recommended and based on level of exposure. Use of additional PPE such as shoe coverings, gauntlets, hood, or head covering may be necessary. Consult your site safety staff for guidance.

EXPOSURE LIMIT VALUES

INGREDIENT	CAS NUMBER	ACGIH TLV (TWA)	OSHA PEL (TWA)
Starch	9005-25-8	10 mg/m^3	15 mg/m^3
Sucrose	57-50-1	10 mg/m^3	15 mg/m^3
Glycerin	56-81-5	10 mg/m^3	15 mg/m^3

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

FORM: Chewable tablet
COLOR: Light to dark brown
ODOR: Odor unknown
SOLUBILITY:
Water: CBPI: <0.001 mg/ml
Acetone: CBPI: 300 - 400 mg/ml
DMSO: CBPI: >700 mg/ml
Ethanol: CBPI: 25 - 50 mg/ml
PARTITION COEFFICIENT (log Pow): CBPI: 4 - 5

ADDITIONAL INFORMATION: Density: 1.3 g/ml

See Section 5 for flammability/explosivity information.

SECTION 10. STABILITY AND REACTIVITY

STABILITY/ REACTIVITY:
Stable under normal conditions.

INCOMPATIBLE MATERIALS / CONDITIONS TO AVOID:
Strong acids. Strong bases. Strong Oxidizers.

HAZARDOUS DECOMPOSITION PRODUCTS / REACTIONS:
No dangerous decomposition is expected if used according to manufacturer's specifications.

SECTION 11. TOXICOLOGICAL INFORMATION

The information presented below pertains to the following individual ingredients, and not to the mixture(s).

ACUTE TOXICITY DATA

INHALATION:
No mortalities were reported in rats (0/6) following a 4-hour exposure to polyethylene glycol vapors generated at 170 deg C; however, mortality was observed in all rats (6/6) following an 8-hour exposure to polyethylene glycol vapors generated at 170 deg C.

Glycerin: Inhalation LC50 (1hr): >570 mg/m^3 [>0.57 mg/L] (rat)

SKIN:
CBPI Dermal LD50: >2000 mg/kg (Rat).
CBPI was not irritating to rabbit skin.

Polyethylene glycols (200-9000 g/mol): Dermal LD50: >20 g/kg (unspecified species).
Polyethylene glycol was not irritating to the skin of rabbits and guinea pigs.
Polyethylene glycol was not irritating in a human patch test.

Glycerin: Skin LD50: >10,000 mg/kg (rabbit)
Glycerin was slightly irritating to the skin of rabbits.

EYE:
CBPI was not irritating to rabbit eyes.

Polyethylene glycols did not produce appreciable eye irritation in rabbits.

Glycerin was slightly irritating to the eyes of rabbits.

ORAL:
CBPI: Oral LD50: >2000 mg/kg (rat)

Polyethylene glycol 300: Oral LD50: 17 to 39 g/kg (rat, mouse, guinea pig, rabbit) Polyethylene glycol 400: Oral LD50: 16-44 g/kg (rat, guinea pig, rabbit)

Glycerin: Oral LD50: 12,600 mg/kg (rat)

Sucrose: Oral LD50: 29,700 mg/kg (rat)
Clinical signs of toxicity observed include hypokinesia, prostration, cyanosis, convulsions, abdominal bloating, and diarrhea. Death results from respiratory failure.

DERMAL AND RESPIRATORY SENSITIZATION:
CBPI was not sensitizing to guinea pig skin.

Polyethylene glycols did not produce skin sensitization in guinea pigs.

REPEAT DOSE TOXICITY DATA

SUBCHRONIC / CHRONIC TOXICITY:
In a 90 day study of CBPI in rats, the NOAEL was established orally at the highest dose of 400 mg/kg/body weight/day. In a 90 day study in rats, the NOAEL was established dermally at the highest dose of 500 mg/kg/body weight/day The liver is the main elimination organ of CBPI and a sensitive target for effects as reflected by increased liver enzyme activity in blood plasma with decreased lipid and protein concentration, increased organ weight and increased hepatocellular fatty change as the main functional endpoints in rats. In the absence of any indicator of liver injury (Kupffer cell proliferation, necrosis, apoptosis, fibrosis, other degenerative changes, etc.) these changes are considered to represent reversible metabolic effects and hence are of non-adverse character.

Polyethylene glycol 400 produced no adverse effects in dogs and rats fed 2% in the diet for one or two years, respectively. Repeated dermal exposure to polyethylene glycol 300 for an eight-week period had no effect on mice. Repeated inhalation exposure to 1008 mg/m^3 of a higher molecular weight polyethylene glycol increased lung weight, and also produced reversible increases in neutrophil counts in male rats.

Glycerin caused calcification in the renal tubules in rats given 5% concentration of glycerin in the drinking water for 6 months.

REPRODUCTIVE / DEVELOPMENTAL TOXICITY:
In prenatal development toxicity studies of CBPI in rats (embryogenisis pilot and pivotal) the final NOEL was 100 mg/kg/body weight/day in maternal and fetal organisms. No teratogenicity at up to the limit dose of 1000 mg/kg/body weight/day, and no effects on embryo or fetus below maternal toxic dose levels were recorded.

Polyethylene glycol 200 was developmentally toxic in mice, causing malformations and other fetotoxicity, but elicited no similar response in rats at higher doses.

Glycerin injected into the testes of rats suppressed sperm production; however, oral administration of 100 mg/kg had no effect on fertility.

Sucrose produced fetal skeletal changes in guinea pigs exposed to high concentrations (5 to 10 g/kg); however, no effects were seen in rats exposed to 10 g/kg/day.

MUTAGENICITY / GENOTOXICITY:
CBPI was negative in a bacterial reverse mutation (Ames) study, a mouse lymphoma in vitro study, a chromosome aberration in vitro study, and a mouse erythrocyte micronucleus in vivo study.

Polyethylene glycol was negative in a bacterial mutagenicity study (Ames), results were inconclusive in a bacterial DNA repair study.

Glycerin was negative in a bacterial mutagenicity study (Ames). Glycerin was positive in chromosome aberration studies in rat bone marrow and sperm cells; however, it was negative in an occupational cytogenetics chromosome aberration study.

Sucrose was negative in a variety of mutagenicity assays.

CARCINOGENICITY:
Sucrose was not carcinogenic in mice and rats exposed to 10% in the diet for 18 months; however, sucrose showed tumor promoting activity in mice.

SECTION 12. ECOLOGICAL INFORMATION

There are no data for the final product or its formulation(s). The information presented below pertains to the following ingredient(s).

ECOTOXICITY DATA

INGREDIENT ECOTOXICITY

CBPI:
96-hr LC50 (Common carp): 2 mg/l
48-hr EC50 (Daphnia magna): 0.0001 - 0.01 mg/l
72-hr EC50 (P. subcapitata): >10 mg/l

Polyethylene glycol: EC50 (daphnid): 22,100 mg/L
Polyethylene glycol: LC50 (fathead minnow): 58,900 mg/L

Glycerin: 8-day EC50 (algae): 2900 mg/L
Glycerin: 96-hr LC50 (trout): 50-67 mg/L
Glycerin: 96-hr LC50 (goldfish): >5000 mg/L

ENVIRONMENTAL DATA

Hydrolysis Rate Results:	Hydrolysis Half-life: CBPI: >1 year (25 deg C) at pH 4, 7, and 9
Partition Coefficient (log Pow) Results:	CBPI: 4.5
Aerobic Biodegradation(soil) Results:	CBPI: DT50: 60 days
Soil Adsorption/Desorption Results:	log Koc: CBPI: 4190 - 6255

OTHER INGREDIENT ENVIRONMENTAL DATA:

CBPI: Bioconcentration Factor (BCF): 27

Polyethylene glycol is expected to be readily biodegradable.

SECTION 13. DISPOSAL CONSIDERATIONS

MATERIAL WASTE:
Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations. Incineration is the preferred method of disposal, when appropriate. Operations that involve the crushing or shredding of waste materials or returned goods must be handled to meet the recommended exposure limit(s).

PACKAGING AND CONTAINERS:
Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations.

SECTION 14. TRANSPORT INFORMATION

Consult current regulatory guidelines for the appropriate transportation classification and labeling of this material. Refer to site-specific procedures and requirements for additional guidance.

DOT CLASSIFICATION:

Non-regulated per 49 CFR 171.4(c) for ground shipments of non-bulk packagings. Bulk packagings greater than 400 kg each are regulated as UN 3077. Shipment by ground under DOT is non-regulated, however, it may be shipped per the hazard classification below to facilitate multi-modal transport involving ICAO (IATA) or IMO.

IATA/ICAO CLASSIFICATION:

Proper Shipping Name:	Environmentally hazardous substance, solid, n.o.s. (Isoxazoline derivative)
Hazard Class:	9
UN Number:	UN 3077
Packing Group:	III

ADR CLASSIFICATION:

Per ADR special provision 601, as a pharmaceutical product (medicine) ready for use, this material is not regulated as a dangerous good for transport within Europe.

Proper Shipping Name:	Environmentally hazardous substance, solid, n.o.s. (Isoxazoline derivative)
Hazard Class:	9

UN Number: UN 3077
Packing Group: III
Classification Code: M7

IMDG/IMO CLASSIFICATION:

Proper Shipping Name: Environmentally hazardous substance, solid, n.o.s. (Isoxazoline derivative)
Hazard Class: 9
UN Number: UN 3077
Packing Group: III

SECTION 15. REGULATORY INFORMATION

TSCA LISTING

INGREDIENT	TSCA
Starch	X
Polyethylene Glycol	X
Sucrose	X
Glycerin	X

Substances not included in the table above are TSCA exempt or not regulated under TSCA.

U.S. STATE REGULATIONS

INGREDIENT	California Proposition 65	CARTK	NJRTK	CTRTK	MARTK
Starch					X
Sucrose					X
Glycerin			3319		X

INGREDIENT	PARTK	MNRTK	MIRTK	RIRTK
Starch	X	X		X
Polyethylene Glycol		X		
Sucrose	X	X		X
Glycerin	X	X		X

Fields in the above tables that do not contain data indicate that those materials have not been listed by local regulations.

X: Listed on applicable state hazardous substance or right-to-know lists.

SECTION 16. OTHER INFORMATION

Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained therein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequence of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s).

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