SAFETY DATA SHEET

Prepared to U.S. OSHA, CMA, ANSI, Canadian WHMIS Standards, European Union CLP EC 1272/2008 and the Global Harmonization Standard

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY UNDERTAKING

PRODUCT IDENTIFIER/TRADE/MATERIAL NAME: CANASA® (Mesalamine) SUPPOSITORY

DESCRIPTION: Mesalamine Suppositories
RELEVANT USE of the SUBSTANCE: Human Pharmaceutical/Anti-Inflammatory
USES ADVISED AGAINST: Non-Pharmaceutical Use
CHEMICAL NAME: For Active Ingredient: 5-amino-2-hydroxybenzoic acid
CHEMICAL FAMILY: For Active Ingredient: Aminosalicylate
FORMULA: For Active Ingredient: $C_7H_7NO_3$
HOW SUPPLIED: 1000 mg: NDC:58914-501-56: 30 in 1 box; NDC:58914-501-42: 42 in 1 box; NDC:58914-501-33: 3 in 1 box; NDC:58914-501-18: 1080 in 1 bag

SUPPLIER OF THE SAFETY DATA SHEET

RESPONSIBLE PARTY U.S.:	**Actavis, Inc.**
U.S. ADDRESS:	400 Interpace Parkway, Morris Corporate Center III Parsippany, NJ 07054, USA
U.S. BUSINESS PHONE/GENERAL SDS INFORMATION:	1-800-272-5525
RESPONSIBLE PARTY EUROPE:	
EUROPEAN ADDRESS:	
EUROPEAN BUSINESS PHONE:	
EMERGENCY PHONE (U.S./NORTH AMERICA):	CHEMTREC: 1-800-424-9300 (24 hours) U.S., Canada, Puerto Rico
EMERGENCY PHONE (OUTSIDE U.S.):	CHEMTREC: +1-703-527-3887 (24 hours) Outside North America
Email:	SDS@Actavis.com

NOTE: ALL United States Occupational Safety and Health Administration Standard (29 CFR 1910.1200), U.S. State equivalent Standards, Canadian WHMIS [Controlled Products Regulations], EU Directives through EC 1907: 2006, and European Union CLP EC 1272/2008, required information is included in appropriate sections based on the U.S. ANSI Z400.1-2010 format. This product has been classified in accordance with the hazard criteria of the countries listed above.

DATE OF PREPARATION: August 30, 2014 **DATE OF REVISION:** New

2. HAZARDS IDENTIFICATION

EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

EU 67/548/EEC LABELING AND CLASSIFICATION: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

EMERGENCY OVERVIEW:

Product Description: This product is supplied as bullet shaped, light tan to grey suppositories.

Health Hazards: Accidental ingestion may be harmful. Inhalation and eye contact may cause irritation. In therapeutic use, the most common adverse reactions reported have included headache, nausea, dizziness, fever, rash, acne, and worsening of ulcerative colitis. Additional symptoms related to rectal administration of the drug are not relevant to workplace exposure. Other adverse effects reported have included renal damage and hypersensitivity reactions, including cardiac hypersensitivity reactions. More information on adverse effects from therapeutic use is described in Section 11 (Toxicological Information).

Flammability Hazards: This product is combustible and may ignite if exposed to high temperature for a prolonged period. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon and nitrogen oxides).

Reactivity Hazards: This product is not reactive.

Environmental Hazards: Large quantities released to the aquatic and terrestrial environment may have an adverse effect.

Other Hazards: No other hazard information currently known.

Emergency Considerations: Emergency responders should wear appropriate protection for situation to which they respond.

3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	% w/w	LABEL ELEMENTS EU Classification (67/548/EEC) GHS & EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements/Symbol
ACTIVE INGREDIENT:				
Mesalamine 5-amino-2-hydroxybenzoic acid	89-57-6	200-374-7	Proprietary	SELF-CLASSIFICATION: EU 67/548 Classification: Harmful, Irritant Risk Phrase Codes: R22, R36/37/39 Hazard Symbols: Xn/Xi GHS and EU 1272/2008 Classification: Acute Oral Toxicity Cat. 4, Skin Irritation Cat. 2, Eye Irritation Cat. 2A, STOT (Inhalation-Respiratory Irritation) Cat. 3 Hazard Codes: H302, H315, H319, H335 Hazard Symbol/Pictogram: GHS07
EXCIPIENTS:				
Hard Fat, NF Triglyceride mixture	Mixture	Mixture	Proprietary	EU 67/548 Classification: Not Applicable GHS and EU 1272/2008 Classification: Not Applicable

See Section 15 for full classification.

4 FIRST-AID MEASURES

PROTECTION OF FIRST AID RESPONDERS: First-aid responders should not attempt to treat victims of exposure to this material without adequate personal protective equipment. Rescuers should be taken for medical attention, if necessary.

DESCRIPTION OF FIRST AID MEASURES: Upon contact of this material with skin, eyes, or mucous membranes, immediately decontaminate by flushing with water for at least 20 minutes. Remove contaminated clothing and shoes. Take a copy of this SDS to health professional with victim. Wash clothing and thoroughly clean shoes before reuse.

Inhalation: Due to the form of this product, inhalation is not a likely route of exposure. If somehow this product is inhaled, remove victim to fresh air. If necessary, use artificial respiration to support vital functions. Seek medical attention if adverse effect occurs after removal to fresh air.

Skin Exposure: Basic hygiene should prevent any problems. If the product contaminates the skin, and adverse effect occurs, begin decontamination with running water. Minimum flushing is for 20 minutes. Do not interrupt flushing. Remove exposed or contaminated clothing, taking care not to contaminate eyes. Seek medical attention if adverse effect occurs after flushing.

Eye Exposure: If this product enters the eyes, open victim's eyes while under gently running water. Use sufficient force to open eyelids. Have victim "roll" eyes. Minimum flushing is for 20 minutes. Do not interrupt flushing. Seek immediate medical attention after flushing if adverse effect occurs.

Ingestion Exposure: If this product is swallowed, CALL PHYSICIAN OR POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. If professional advice is not available, do not induce vomiting. Rinse mouth with water immediately. Victim should drink large quantities of water. If milk is available, victim should drink it after drinking water. Never induce vomiting or give diluents (milk or water) to someone who is unconscious, having convulsions, or unable to swallow.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: In therapeutic use, liver disease, renal impairment, upper gastrointestinal obstruction or cardio conditions such as myocarditis and pericarditis may be aggravated by exposure. Workplace exposure may also aggravate these conditions. Persons who may have hypersensitivity reactions to sulfazines, salicylates or aminosalicylates or other disorders described in Section 11 (Toxicological Information) may experience aggravation upon exposure.

INDICATION OF IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT IF NEEDED: Treat symptoms and eliminate exposure. Persons developing hypersensitivity reactions should receive immediate medical attention. There is no specific antidote for Mesalamine treatment should be symptomatic and supportive. This may include prevention of further gastrointestinal tract absorption, correction of fluid electrolyte imbalance, and maintenance of adequate renal function.

5. FIRE-FIGHTING MEASURES

FLASHPOINT: Not determined.

AUTOIGNITION TEMPERATURE: Not applicable.

FLAMMABLE LIMITS & METHOD OF DETERMINATION (in air by volume, %): Not applicable.

FIRE EXTINGUISHING MEDIA: Use extinguishing media appropriate for surrounding fire.

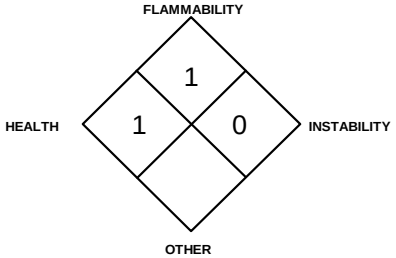
UNSUITABLE EXTINGUISHING MEDIA: None known.

SPECIFIC HAZARDS ARISING FROM THE PRODUCT: This product is not combustible and may ignite if exposed to high temperature for a prolonged period. If involved in a fire, the water component may evaporate and the residual may ignite. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon and nitrogen oxides).

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

NFPA RATING



Hazard Scale: **0** = Minimal **1** = Slight **2** = Moderate **3** = Serious **4** =

5. FIRE-FIGHTING MEASURES (Continued)

SPECIAL PROTECTIVE ACTIONS FOR FIRE-FIGHTERS: Incipient fire responders should wear eye protection. Structural firefighters must wear Self-Contained Breathing Apparatus (SCBA) and full protective equipment. If protective equipment is contaminated by this product, it should be thoroughly washed with running water prior to removal of SCBA respiratory protection. Firefighters whose protective equipment becomes contaminated should thoroughly shower with warm, soapy water and should receive medical evaluation if they experience any adverse effects.

6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS: In the event of a spill, clear the area and protect people. The atmosphere must have levels of components lower than those listed in Section 8, (Exposure Controls and Personal Protective Equipment) if applicable, and have at least 19.5 percent oxygen before personnel can be allowed into the area without Self-Contained Breathing Apparatus (SCBA). Monitor area and confirm levels are bellow exposure limits given in Section 8 (Exposure Controls-Personal Protection), if applicable, before non-response personnel are allowed into the spill area. Spills may be slippery.

PROTECTIVE EQUIPMENT:

Small Spills: For incidental spills (e.g., several suppositories), wear double latex or nitrile disposable gloves and eye protection.

Large Spills: For large spills (e.g., 1 liter or more), protective apparel should be used with a respirator when there is any danger of aerosols being generated. Minimum Personal Protective Equipment should be rubber gloves, rubber boots, face shield, and Tyvek suit. Minimum level of personal protective equipment for releases in which the level of oxygen is less than 19.5% or is unknown must be **Level B: triple-gloves (rubber gloves and nitrile gloves over latex gloves), chemical resistant suit and boots, hard hat, and Self-Contained Breathing Apparatus.**

METHODS FOR CLEANUP AND CONTAINMENT:

Small Spills: Absorb up spilled material with damp sponge, polypads or other suitable material.

Large Spills: Trained personnel following pre-planned procedures should handle non-incidental releases. Access to the spill areas should be restricted. Absorb spilled product carefully, avoiding the generation of aerosols onto polypads or other non-reactive absorption.

All Spills: Decontaminate the area of the spill thoroughly using detergent and water. Place all spill residue in an appropriate container and seal. Do not mix with wastes from other materials. If necessary, discard contaminated response equipment or rinse with soapy water before returning such equipment to service. Dispose of in accordance with applicable international, national, state, and local procedures (see Section 13, Disposal Considerations).

ENVIRONMENTAL PRECAUTIONS: Prevent material from entering sewer or confined spaces, waterways, soil or public waters. Do not flush to sewer. For spills on water, contain, minimize dispersion and collect.

7. HANDLING and USE

PRODUCT PREPARATION INSTRUCTIONS FOR MEDICAL PERSONNEL: Handle this material following standard medical practices and following the recommendations presented on the Package Insert.

PRECAUTIONS FOR SAFE HANDLING: All employees who handle this product should be trained to handle it safely. Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this compound, and during patient administration. As with all chemicals, avoid getting this product ON YOU or IN YOU. Wash thoroughly after handling this product or equipment and containers that contain this product. Do not eat or drink while using this product. Avoid breathing airborne mists or spray generated by this product. Ensure this product is used with adequate ventilation (refer to Section 8, Exposure Controls-Personal Protection). Remove contaminated clothing immediately. Keep container tightly closed when not in use. Open containers slowly on a stable surface in areas that have been designated for use of this product. Wipe down areas in which this product is used, so that product does not accumulate. Empty containers may contain residual material; therefore, empty containers should be handled with care.

CONDITIONS FOR SAFE STORAGE: Containers of this product must be properly labeled. Store containers in a cool, dry location, away from direct sunlight, sources of intense heat or other sources of ignition or where freezing is possible. Store at 20-25°C (68-77°F) and away from moisture, humidity and light. Product should be stored in secondary containers or in a diked area, as appropriate. Store away from incompatible materials (see Section 10, Stability and Reactivity).

SPECIFIC END USE(S): This product is a human pharmaceutical. Follow all industry standards for use of this product.

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear latex or butyl rubber (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. Wipe equipment down with damp sponge or polypad.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

EXPOSURE LIMITS/CONTROL PARAMETERS:

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures. During decontamination of work surfaces, workers should wear the same equipment recommended in Section 6 (Accidental Release Measures) of this SDS.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

EXPOSURE LIMITS/CONTROL PARAMETERS (continued):

Occupational/Workplace Exposure Limits/Guidelines:

CHEMICAL NAME	CAS #	EXPOSURE LIMITS IN AIR							
		ACGIH-TLVs		OSHA-PELs		NIOSH-RELs		NIOSH	OTHER
		TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	IDLH mg/m^3	mg/m^3
Mesalamine	89-57-6	NE	NE	NE	NE	NE	NE	NE	Actavis OEL: 800 $\mu g/m^3$
Hard Fat (mixture of triglycerides)		NE	NE	NE	NE	NE	NE	NE	NE

NE = Not Established.

International Occupational Exposure Limits: Currently, the no additional exposure limits have been established by various countries for components of this product. The exposure limits given may not be the most current; individual country authorities should be contacted to check on more current limits.

PERSONAL PROTECTIVE EQUIPMENT: Use of personal protective equipment must be in compliance with U.S. OSHA 29 CFR Subpart I (beginning at 1910.132), Canadian CSA Standards Z94.4-02 and Z94.3-02, EU EN 529:2005, CEN/TR 15419:2006, and CR 13464:1999. Please reference applicable regulations and standards for relevant details.

Respiratory Protection: A respirator is not required for routine conditions of use with adequate engineering controls. A full-face Air-Purifying Respirator with high-efficiency particulate filter or a Supplied-Air Respirator must be worn during operations where engineering controls are not sufficient, large spill cleanup, or when processing generates airborne aerosols. If respiratory protection is needed, use only respiratory protection authorized under appropriate regional regulations.

Eye Protection: During operations in which mists or sprays may be generated, splash goggles or safety glasses should be considered.

Hand Protection: During manufacture or other similar industrial operations, wear the appropriate hand protection for the process. Use double gloves for spill response, as stated in Section 6 (Accidental Release Measures) of this SDS.

Body Protection: Use appropriate protective clothing for the task (e.g., lab coat, etc.)

9. PHYSICAL and CHEMICAL PROPERTIES

The following information is for the product.

FORM: Bullet shaped suppositories.
COLOR: As described in Section 2.
ODOR: No odor.
ODOR THRESHOLD: Not available.
HOW TO DETECT THIS SUBSTANCE (identification properties): The appearance of this product is a distinguishing characteristic.

The following information is for the Mesalamine active ingredient.

FORM: Needle-shaped crystals.
COLOR: Light tan to pink-colored.
MOLECULAR FORMULA: $C_7H_7NO_3$
MOLECULAR WEIGHT: 153.14
ODOR: Slight.
ODOR THRESHOLD: Not available.
BOILING POINT @ 760 mmHg: 1250.6°C (2283.1°F) [predict.]
MELTING POINT: 280-283°C (536-541°F)
VAPOR PRESSURE (air = 1) @ 25°C: 0.0 mmHg [predict.]
SPECIFIC GRAVITY (water = 1): Not available.
EVAPORATION RATE (nBuAc = 1): Not applicable.
pH: 4.0-5.0 (susp. 1 g/40 mL distilled water)
FLASH POINT: 560°C (1040°F) [predict.]
DECOMPOSITION TEMPERATURE: ~280°C (~536°F)
SOLUBILITY IN WATER @ 25°C: Slightly soluble.
PARTITION COEFFICIENT: pKa1 (2.3); pKa2 (5.69)
COEFFICIENT WATER/OIL DISTRIBUTION: Log Kow: 0.98 (est.)
OTHER SOLUBILITIES: Slightly soluble in alcohol; more soluble in hot water; soluble in hydrochloric acid; practically insoluble in ethanol, acetone and ether. Dissolves in dilute solutions of alkali hydroxides and dilute hydrochloric acid.

10. STABILITY and REACTIVITY

CHEMICAL STABILITY: This product is stable under normal conditions of storage.
HAZARDOUS DECOMPOSITION PRODUCTS: ***Combustion:*** If exposed to extremely high temperatures, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon and nitrogen oxides). ***Hydrolysis:*** None known.
INCOMPATIBLE MATERIALS: This compound is incompatible with strong oxidizers, strong acids.
POSSIBILITY OF HAZARDOUS REACTIONS/ POLYMERIZATION: No data available.
CONDITIONS TO AVOID: Avoid heat, light, and contact with incompatible chemicals.

11. TOXICOLOGICAL INFORMATION

SYMPTOMS OF EXPOSURE BY ROUTE OF EXPOSURE: The health hazard information provided below is pertinent to employee handling in an occupational setting. The following paragraphs describe the symptoms of exposure by route of exposure.

Inhalation: Although unlikely due to the form of the product, inhalation of airborne aerosols generated by this product may irritate the nose, throat, and lungs. Some available information indicates penicillums can cause respiratory sensitization and allergic reaction.

Skin Contact: Contact with the skin may cause irritation. Prolonged or repeated skin contact may cause dermatitis (dry, red skin).

Eye Contact: Contact with the eyes of aerosols generated by this product may cause irritation, redness, and tearing.

Skin Absorption: No specific data is available on potential absorption of this material through intact skin.

SYMPTOMS OF EXPOSURE BY ROUTE OF EXPOSURE (continued):

Ingestion: Ingestion is not a significant route of occupational exposure. Symptoms of acute ingestion may include those described under 'Other Health Effects'.

Injection: Though not anticipated to be a significant route of exposure for this product, injection (via punctures or lacerations by contaminated objects) may cause redness at the site of injection. Symptoms may also include those described under 'Other Health Effects'.

OTHER POTENTIAL HEALTH EFFECTS-Therapeutic Doses: In therapeutic use, the most common adverse reactions reported have included headache, nausea, dizziness, fever, rash, acne, and worsening of ulcerative colitis. Additional symptoms related to rectal administration of the drug are not relevant to workplace exposure. Other adverse effects reported have included renal damage and hypersensitivity reactions, including cardiac hypersensitivity reactions. In therapeutic use the following additional adverse effects described by body system have included:

- ***Blood System:*** Acute failure of bone marrow to make new blood cells, including white blood cells, blood platelet decrease.
- ***Body as a Whole:*** Drug fever, fatigue, lupus-like syndrome (auto-immune disorder).
- ***Cardiovascular System:*** Inflammation of heart muscle, and pericardium (sac surrounding heart), fluid around the heart.
- ***Central Nervous and Peripheral System:*** Dizziness, headache, Guillain-Barre syndrome, peripheral neuropathy, inflammatory disease causing injury to the spinal cord with varying degrees of weakness, sensory alterations, and autonomic dysfunction (the part of the nervous system that controls involuntary activity, such as the heart, breathing, the digestive system, and reflexes).
- ***Eyes:*** Eye swelling.
- ***Gastrointestinal Disorders:*** Abdominal cramps, abdominal distension, anal itching, ano-rectal discomfort, constipation, discolored feces, flatulence, frequent bowel movements, gastrointestinal bleeding, mucus in stools, nausea, painful defecation, pancreatitis, severe, episodic, rectal and digestive system pain, rectal discharge, feeling that you need to have a bowel movement, stomach discomfort, vomiting.
- ***Liver***: Cholestatic jaundice, hepatitis, jaundice, Kawasaki-like syndrome including changes in liver enzymes, liver necrosis, liver failure.
- ***Renal System:*** Interstitial nephritis (form of kidney disease).
- ***Reproductive Disorders:*** Reversible low sperm concentration.
- ***Respiratory System:*** Hypersensitivity pneumonitis (including allergic inflammation of the alveoli, white blood cell disorder causing respiratory infection, pneumonitis causing progressive scarring of both lungs).
- ***Skin:*** Hair loss, tissue swelling, tender, red bumps (nodules) under the skin, itching, rash, hives, red, scaly skin, pyoderma gangrenosum (skin condition, causing tissue to become necrotic, leading to deep ulcers that usually occur on the legs).

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

HEALTH HAZARD	(BLUE)	1
FLAMMABILITY HAZARD	(RED)	1
PHYSICAL HAZARD	(YELLOW)	0

PROTECTIVE EQUIPMENT

EYES	RESPIRATORY	HANDS	BODY
	SEE SECTION 8		SEE SECTION 8

For Routine Industrial Use and Handling Applications

Hazard Scale: **0** = Minimal **1** = Slight **2** = Moderate **3** = Serious **4** = Severe * = Chronic hazard

HEALTH EFFECTS OR RISKS FROM EXPOSURE: An Explanation in Lay Terms. Exposure to this product may cause the following health effects:

Acute: Prolonged contact with this product may cause irritation via skin or eye contact.

Chronic: Repeated skin contact may cause dermatitis (dry, red skin). Chronic exposure may cause adverse symptoms as described under 'Other Health Effects'.

TARGET ORGANS:

Acute: *Industrial Exposure*: Skin, eyes. *Therapeutic Doses*: Gastrointestinal system.

Chronic: *Industrial Exposure*: Skin. *Therapeutic Doses*: Systems given under "Other Potential Health Effects'.

IRRITANCY OF PRODUCT: This product may irritate contaminated tissue if contact is prolonged.

SENSITIZATION TO THE PRODUCT: In therapeutic use, Mesalamine-induced cardiac hypersensitivity reactions (myocarditis and pericarditis) have been reported, especially in persons with hypersensitivity to sulfasalazine. Additionally, reports of facial and extremity swelling, itching, hives and hair loss have occurred.

TOXICITY DATA: Currently the following toxicity data are available for the active ingredient. Additional data are available, for excipients, but are not presented in this SDS. Contact Actavis for more information.

MESALAMINE:

TDLo (Oral-Woman) 8760 mg/kg/1 year-intermittent: Behavioral: anorexia (human), muscle weakness; Kidney/Ureter/Bladder: changes in tubules (including acute renal failure, acute tubular necrosis)

TDLo (Oral-Woman) 5400 mg/kg/90 days-intermittent: Gastrointestinal: changes in structure or function of endocrine pancreas

TDLo (Oral-Woman) 80 mg/kg/1 days-intermittent: Cardiac: pulse rate; Vascular: BP lowering not characterized in autonomic section

TDLo (Oral-Woman) 21,800 mg/kg/39 weeks-intermittent: Lungs, Thorax, or Respiration: fibrosis, focal (pneumoconiosis), respiratory depression; Blood: eosinophilia

MESALAMINE (continued):

TDLo (Oral-Woman) 8 mg/kg: Behavioral: headache; Gastrointestinal: hypermotility, diarrhea; Nutritional and Gross Metabolic: body temperature increase

TDLo (Oral-Man) 321 mg/kg/15 days-intermittent: Skin and Appendages: photosensitivity (after systemic exposure)

TDLo (Oral-Man) 6857 mg/kg/17 weeks-intermittent: Gastrointestinal: nausea or vomiting; Liver: jaundice, cholestatic

TDLo (Oral-Man) 51 mg/kg/5 days-intermittent: Gastrointestinal: hypermotility, diarrhea; Skin and Appendages: dermatitis, other (after systemic exposure); Nutritional and Gross Metabolic: body temperature increase

TOXICITY DATA (continued):

MESALAMINE (continued):

TDLo (Oral-Man) 2057 mg/kg/17 weeks-intermittent: Blood: agranulocytosis; Nutritional and Gross Metabolic: body temperature increase

TDLo (Oral-Man) 6.86 gm/kg/16 weeks-intermittent: Gastrointestinal: nausea or vomiting; Liver: jaundice (or hyperbilirubinemia) hepatocellular; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: multiple enzyme effects

TDLo (Oral-Man) 503 mg/kg/26 weeks-intermittent: Gastrointestinal: other changes; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol); Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: multiple enzyme effects

TDLo (Oral-Child) 20 mg/kg: Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol)

TDLo (Unreported-Child) 400 mg/kg/10 days-continuous: Gastrointestinal: nausea or vomiting; Skin and Appendages: dermatitis, allergic (after systemic exposure); Nutritional and Gross Metabolic: body temperature increase

LD_{50} (Oral-Rat) 2800 mg/kg: Behavioral: somnolence (general depressed activity), food intake (animal); Gastrointestinal: other changes

LD_{50} (Oral-Mouse) 3370 mg/kg

LD_{50} (Skin-Rabbit) > 5 gm/kg

MESALAMINE (continued):

LD_{50} (Intraperitoneal-Rat) 100 mg/kg: Behavioral: analgesia

LD_{50} (Intraperitoneal-Rat) 1 gm/kg: Behavioral: convulsions or effect on seizure threshold; Kidney/Ureter/Bladder: other changes in urine composition; Skin and Appendages: hair

LD_{50} (Intraperitoneal-Mouse) 469 mg/kg

LDLo (Oral-Monkey) 3 gm/kg: Sense Organs and Special Senses (Eye): ptosis; Behavioral: somnolence (general depressed activity); Kidney/Ureter/Bladder: hematuria

TDLo (Oral-Rat) 36,400 mg/kg/13 weeks-intermittent: Kidney/Ureter/Bladder: urine volume increased, changes in bladder weight; Blood: normocytic anemia

TDLo (Oral-Mouse) 525 mg/kg/7 days-intermittent: Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation

TDLo (Rectal-Rat) 840 mg/kg/1 weeks-intermittent: Gastrointestinal: other changes; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: other oxidoreductases, Metabolism (Intermediary): effect on inflammation or mediation of inflammation

TDLo (Rectal-Rat) 2100 mg/kg/3 weeks-intermittent: Gastrointestinal: other changes

OTHER ANIMAL TOXICITY DATA: Toxicology studies of Mesalamine were conducted in rats, mice, rabbits and dogs, and the kidney was the main target organ of toxicity. In rats, adverse renal effects were observed at a single oral dose of 600 mg/kg (about 3.2 times the recommended human intra-rectal dose, based on body surface area) and at IV doses of >214 mg/kg (about 1.2 times the recommended human intra-rectal dose, based on body surface area). In a 13-week oral gavage toxicity study in rats, papillary necrosis and/or multifocal tubular injury were observed in males receiving 160 mg/kg (about 0.86 times the recommended human intra-rectal dose, based on body surface area) and in both males and females at 640 mg/kg (about 3.5 times the recommended human intra-rectal dose, based on body surface area). In a combined 52-week toxicity and 127-week carcinogenicity study in rats, degeneration of the kidneys and hyalinization of basement membranes and Bowman's capsule were observed at oral doses of 100 mg/kg/day (about 0.54 times the recommended human intra-rectal dose, based on body surface area) and above. In a 14-day rectal toxicity study of Mesalamine suppositories in rabbits, intra-rectal doses up to 800 mg/kg (about 8.6 times the recommended human intra-rectal dose, based on body surface area) was not associated with any adverse effects. In a six-month oral toxicity study in dogs, doses of 80 mg/kg (about 1.4 times the recommended human intra-rectal dose, based on body surface area) and higher caused renal pathology similar to that described for the rat. In a rectal toxicity study of Mesalamine suppositories in dogs, a dose of 166.6 mg/kg (about 3.0 times the recommended human intra-rectal dose, based on body surface area) produced chronic nephritis and pyelitis. In the 12-month eye toxicity study in dogs, keratoconjunctivitis sicca (KCS) occurred at oral doses of 40 mg/kg (about 0.72 times the recommended human intra-rectal dose, based on body surface area) and above.

CARCINOGENIC POTENTIAL: The following information is available for the active ingredient.

Mesalamine was not carcinogenic at dietary doses of up to 480 mg/kg/day in rats and 2000 mg/kg/day in mice, which are about 2.9 and 6.1 times the maximum recommended maintenance dose of Mesalamine of 1.6 g/day or 26.7 mg/kg/day, based on 60 kg body weight, respectively, based on body surface area.

The remaining component is not found on the following lists: U.S. EPA, U.S. NTP, U.S. OSHA, U.S. NIOSH, GERMAN MAK, IARC, or ACGIH and therefore are neither considered to be nor suspected to be cancer-causing agents by these agencies.

REPRODUCTIVE TOXICITY INFORMATION: There are no adequate and well-controlled studies of Mesalamine in pregnant women; however, when administered therapeutically, Mesalamine is not expected to cause fetal harm when administered to a pregnant woman. In formulated products this material is rated by the FDA for therapeutic risk as Pregnancy Risk Category B (Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester).

Mutagenicity: Mesalamine was negative in the Ames assay for mutagenesis, negative for induction of sister chromatid exchanges (SCE) and chromosomal aberrations in Chinese hamster ovary cells *in vitro*, and negative for induction of micronuclei (MN) in mouse bone marrow polychromatic erythrocytes.

Embryotoxicity/Teratogenicity:

Human Data: Limited published human data on Mesalamine show no increase in the overall rate of congenital malformations. Some data show an increased rate of preterm birth, stillbirth, and low birth weight; however, these adverse pregnancy outcomes are also associated with active inflammatory bowel disease. Furthermore, all pregnancies, regardless of drug exposure, have a background rate of 2 to 4% for major malformations, and 15 to 20% for pregnancy loss. Mesalamine crosses the placenta. In prospective and retrospective studies of over 600 women exposed to Mesalamine during pregnancy, the observed rate of congenital malformations was not increased above the background rate in the general population. Some data show an increased rate of preterm birth, stillbirth, and low birth weight, but it is unclear whether this was due to underlying maternal disease, drug exposure, or both, as active inflammatory bowel disease is also associated with adverse pregnancy outcomes.

Animal Data: No evidence of fetal harm was observed in animal reproduction studies of Mesalamine in rats and rabbits at oral doses approximately 1.9 times (rat) and 3.9 times (rabbit) the recommended human dose. Reproduction studies with Mesalamine were performed during organogenesis in rats and rabbits at oral doses up to 480 mg/kg/day. These Mesalamine doses were about 1.9 times (rat) and 3.9 times (rabbit) the recommended human dose, based on body surface area.

11. TOXICOLOGICAL INFORMATION (Continued)

REPRODUCTIVE TOXICITY INFORMATION (continued):

Reproductive Toxicity: Mesalamine, at oral doses up to 480 mg/kg/day (about 1.9 times the recommended human treatment dose on a body surface area basis), was found to have no effect on fertility or reproductive performance of male and female rats. Mesalamine and its N-acetyl metabolite are present in human milk. In published lactation studies, maternal Mesalamine doses from various oral and rectal formulations and products ranged from 500 mg to 3 g daily. The concentration of Mesalamine in milk ranged from non-detectable to 0.11 mg/L. The concentration of the N-acetyl-5-aminosalicylic acid metabolite ranged from 5 to 18.1 mg/L. Based on these concentrations, estimated infant daily doses for an exclusively breastfed infant are 0 to 0.017 mg/kg/day of Mesalamine and 0.75 to 2.72 mg/kg/day of N-acetyl-5-aminosalicylic acid. Because of the potential for serious adverse reactions in nursing infants, nursing mothers should be advised of these effects and the appropriate action should be taken to prevent exposure.

ACGIH BIOLOGICAL EXPOSURE INDICES (BEIs): Currently, ACGIH Biological Exposure Indices (BEIs) have not been determined for the components of this product.

12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

Some values for the active ingredient are available for the active ingredient, but are not presented in this SDS. Contact Actavis for more information.

MOBILITY IN SOIL: This product has not been tested for mobility in soil.

PERSISTENCE AND BIODEGRADABILITY: This product has not been tested for persistence or biodegradability. Due to high level of organic glycerides, that portion of the product is expected to degrade.

BIO-ACCUMULATIVE POTENTIAL: This product is not expected to present a hazard of bioconcentration.

ECOTOXICITY: No data is available for this product. All releases to terrestrial, atmospheric and aquatic environments should be avoided.

RESULTS OF PBT AND vPvB ASSESSMENT: No Data Available. PBT and vPvB assessments are part of the chemical safety report required for some substances in European Union Regulation (EC) 1907/2006, Article 14.

OTHER ADVERSE EFFECTS: This material has no known ozone depletion potential.

ENVIRONMENTAL EXPOSURE CONTROLS: Controls should be engineered to prevent release to the environment, including procedures to prevent spills, atmospheric release and release to waterways.

13. DISPOSAL CONSIDERATIONS

WASTE TREATMENT/DISPOSAL METHODS: Waste disposal must be in accordance with appropriate Federal, State, and local regulations. Waste containers should be handled with uncontaminated gloves. Reusable equipment should be decontaminated using 0.05M Boric acid solution adjusted to pH 9 with 10 N sodium hydroxide followed by a detergent wash and then clean water rinse or by using a bleach solution (triple wash) and a detergent solution followed by clean water rinse.

PRECAUTIONS TO BE FOLLOWED DURING WASTE HANDLING: Wear proper protective equipment when handling waste materials.

U.S. EPA WASTE NUMBER: Not applicable.

EUROPEAN WASTE CODES: Wastes from Human or Animal Health Care or Related Research: 18 01 08: Medicines Other Than Those Mentioned in 18 01 07.

14. TRANSPORTATION INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION: This product is NOT classified as dangerous goods, per U.S. DOT regulations, under 49 CFR 172.101.

TRANSPORT CANADA: This product is NOT classified as Dangerous Goods, per regulations of Transport Canada.

INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA): This product is not classified as Dangerous Goods, by rules of IATA.

INTERNATIONAL MARITIME ORGANIZATION (IMO): This product is NOT classified as Dangerous Goods, per rules of IMO.

UNITED NATIONS ECONOMIC COMMISSION FOR EUROPE (UNECE): This product is NOT classified by the United Nations Economic Commission for Europe to be dangerous goods.

TRANSPORT IN BULK ACCORDING TO THE IBC CODE: Not applicable.

ENVIRONMENTAL HAZARDS: This product is neither environmentally hazardous according to the criteria of the UN Model Regulations (as reflected in the IMDG Code, ADR, RID, and ADN) nor a marine pollutant according to the IMDG Code and is not listed in Annex III under MARPOL 73/78.

15. REGULATORY INFORMATION

UNITED STATES REGULATIONS:

U.S. SARA Reporting Requirements: The components of this product are not subject to the reporting requirements of Sections 302, 304, and 313 of Title III of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity (TPQ): There are no specific Threshold Planning Quantities for any component of this product. The default Federal SDS submission and inventory requirement filing threshold of 10,000 lb (4,540 kg) therefore applies, per 40 CFR 370.20.

U.S. CERCLA Reportable Quantities (RQ): Not applicable.

15. REGULATORY INFORMATION (Continued)

UNITED STATES REGULATIONS (continued):

U.S. TSCA Inventory Status: This product is regulated under Food and Drug Administration standards; it is not subject to requirements under TSCA.

Other U.S. Federal Regulations: Regulations of the FDA under the Federal Food, Drug and Cosmetic Act are applicable when this material is used in pharmaceutical preparations. Under the Hazard Communication Standard (HCS), Section (b)(5)(ii) drugs are subject to labeling requirements by the FDA under the Federal Food, Drug and Cosmetic Act and are exempt from labeling provisions of the HCS; this section of the HCS exempts only labeling requirements and not requirements for a Safety Data Sheet for drugs.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): No component of this product is on the California Proposition 65 Lists.

CANADIAN REGULATIONS:

Canadian DSL Inventory Status: This product regulated by the Therapeutic Products Programme (TPP) of Health Canada and so it excepted from requirements of the DSL/NDSL Inventory.

Canadian Environmental Protection Act (CEPA) Priorities Substances Lists: The components of this product are not on the CEPA Priorities Substances Lists.

Canadian WHMIS Classification and Symbol: The WHMIS Requirements of the Hazardous Products Act does not apply in respect of the advertising, sale or importation of any cosmetic, device, drug or food within the meaning of the Food and Drugs Act.

EUROPEAN REGULATIONS:

Safety, Health, and Environmental Regulations/Legislation Specific for the Product: When formulated in a finished medicinal product for human use, this material is subject to Directive 2001/83/EC and subsequent amendments to the directive.

Chemical Safety Assessment: No Data Available. The chemical safety assessment is required for some substances according to European Union Regulation (EC) 1907/2006, Article 14.

16. OTHER INFORMATION

U.S. ANSI LABELING (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): WARNING! MAY BE HARMFUL IF ACCIDENTALLY INGESTED. Do not taste or swallow. Avoid contact with skin, eyes, and clothing. Wash thoroughly after handling. Wear gloves, goggles, and appropriate body protection during handling or administration. FIRST-AID: In case of contact, flush skin or eyes with plenty of water. If adverse respiratory reaction occurs from allergic reaction, give oxygen and seek immediate medical attention. If ingested, DO NOT induce vomiting. Seek immediate medical attention. IN CASE OF FIRE: Use water fog, dry chemical, CO_2, or "alcohol" foam. IN CASE OF SPILL: Absorb spilled product with appropriate materials/absorbent. Place residual in appropriate container and seal. Dispose of according to applicable regulations. Consult Safety Data Sheet for additional information.

GLOBAL HARMONIZATION AND EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

EU 67/548/EEC LABELING AND CLASSIFICATION: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

CLASSIFICATION OF COMPONENTS:

CLP Regulation (EC) 1272/2008

Mesalamine: This is a self-classification.

Classification: Acute Oral Toxicity Category 4, Skin Irritation Category 2, Eye Irritation Category 2A, Specific Target Organ Toxicity (Inhalation-Respiratory Irritation) Single Exposure Category 3

Hazard Statements: H302: Harmful if swallowed. H315: Causes skin irritation. H319: Causes serious eye irritation. H335: May cause respiratory irritation.

Other Component: An official classification for this substance has not been published nor is applicable.

67/548/EEC:

Mesalamine: This is a self-classification.

Classification: Harmful

Risk Phrases: R22: Harmful if swallowed. R36/37/38: Irritating to eyes, respiratory system and skin.

Other Component: An official classification for this substance has not been published nor is applicable.

REFERENCES AND DATA SOURCES: Contact the supplier for information.

METHODS OF EVALUATING INFORMATION FOR THE PURPOSE OF CLASSIFICATION: Bridging principles were used to classify this product.

REVISION DETAILS: September 2013: Up-date to include additional active ingredient percentage. Up-date throughout to current classification and format.

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This Safety Data Sheet is offered pursuant to OSHA's Hazard Communication Standard, 29 CFR, 1910.1200. Other government regulations must be reviewed for applicability to this product. To the best of Actavis Laboratories, Inc. knowledge, the information contained herein is reliable and accurate as of this date; however, accuracy, suitability or completeness are not guaranteed and no warranties of any type, either express or implied, are provided. The information contained herein relates only to this specific product. If this product is combined with other materials, all component properties must be considered. Data may be changed from time to time. Be sure to consult the latest edition.