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: CONSTULOSE (LACTULOSE SOLUTION USP)

DESCRIPTION: Lactulose, Fructose, Galactose, Lactose Oral Solution
PRODUCT USE: Human Pharmaceutical
USES ADVISED AGAINST: Non-Pharmaceutical Use
CHEMICAL NAME: For Active Ingredients: Lactulose: 4-O-β-D-Galactopyranosyl-β-D-fructofuranose;
Fructose: (3R,4R,5S)-2,5-bis(hydroxymethyl)oxolane-2,3,4-triol;
Galactose: (2S,3R,4S,5R,6R)-6-(hydroxymethyl)oxane-2,3,4,5-tetrol;
Lactose: β-D-galactopyranosyl-(1→4)-D-glucose
CHEMICAL FAMILY: For Active Ingredient: Lactulose, Lactose: Disaccharide; Fructose, Galactose: Glycosyls
FORMULA: For Active Ingredients: Lactulose, Lactose: $C_{12}H_{22}O_{11}$; Fructose, Galactose: $C_6H_{12}O_6$
HOW SUPPLIED: 10 g/15 mL Lactulose Oral Solution
OTHER DESIGNATIONS: NDC:45963-439-63: 237 mL in 1 bottle; NDC:45963-439-65: 946 mL in 1 bottle

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:	
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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], and European Union CLP EC 1272/2008, required information is included in appropriate sections based on the Global Harmonization Standard format.

DATE OF PREPARATION: September 20, 2015 **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.

EMERGENCY OVERVIEW:

Product Description: This product is a natural-colored solution.

Health Hazards: The chief health hazard associated with exposure during normal use and handling is the potential for irritation from eye contact or by inhalation of mists or sprays. Accidental ingestion may cause stomach pain and diarrhea, especially in persons who are lactose intolerant. In therapeutic use, the most common adverse effects reported have included flatulence or belching and abdominal discomfort such as cramping. More information on adverse effects from is described in Section 11 (Toxicological Information).

Reactivity Hazards: This product is not reactive.

Flammability Hazards: This product is not flammable or combustible. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon, potassium and nitrogen oxides).

Environmental Hazards: Although this product is not expected to cause significant harm if released to the environment, all accidental release should be avoided.

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 GHS Under U.S. OSHA & EU Classification (1272/2008 EC) Hazard Statement Codes
Lactulose	4618-18-2	225-027-7	Proprietary	GHS under U.S. OSHA & EU CLP 1272/2008: No Classification Applicable.
Fructose	57-48-7	200-333-3	Proprietary	GHS under U.S. OSHA & EU CLP 1272/2008: No Classification Applicable.
Galactose	59-23-4	200-416-4	Proprietary	GHS under U.S. OSHA & EU CLP 1272/2008: No Classification Applicable.
Lactose	63-42-3	200-559-2	Proprietary	GHS under U.S. OSHA & EU CLP 1272/2008: No Classification Applicable.
Water, USP	7732-18-5	231-791-2	Proprietary	GHS under U.S. OSHA & EU CLP 1272/2008: No Classification Applicable.

See Section 16 for full classification information.

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: Victim(s) must be taken for medical attention. Remove victim(s) to fresh air, as quickly as possible. Only trained personnel should administer supplemental oxygen and/or cardio-pulmonary resuscitation, when necessary. Take copy of SDS to physician or other health professional with victim(s).

Inhalation: If mists or sprays from this product are 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.

IMPORTANT SYMPTOMS AND EFFECTS: See Sections 2 (Hazard Identification) and 11 (Toxicological Information).

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: In therapeutic use, cardiac arrhythmias and QTc prolongation conditions, liver disorders, moderate or severe renal impairment (creatinine clearance <50 mL/min) or sensitivity to other azole antifungal agents may be aggravated. Persons with these conditions may also have aggravation of these disorders. Workplace exposure may also aggravate these conditions.

INDICATION OF IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT IF NEEDED: Treat symptoms and eliminate exposure. General supportive measures and symptomatic treatment should be followed in all cases of overdosage. Dialysis data are not available for Lactulose. Its molecular similarity to sucrose, however, would suggest that it should be dialyzable.

5. FIRE-FIGHTING MEASURES

FLASH POINT: Not established.

AUTOIGNITION TEMPERATURE: Not applicable.

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

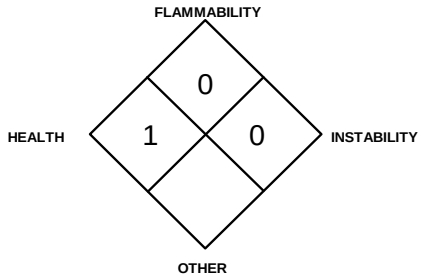
FIRE EXTINGUISHING MEDIA: In the event of a fire, use suppression methods for surrounding materials, including water spray (for cooling), dry extinguishing media, carbon dioxide, foam.

UNSUITABLE FIRE EXTINGUISHING MEDIA: None known.

SPECIFIC HAZARDS ARISING FROM THE PRODUCT: This product is expected to be a combustible liquid that may ignite if highly heated for a prolonged period or if subject to direct flame. When involved in a fire, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon, potassium and nitrogen oxides).

Explosion Sensitivity to Mechanical Impact/Explosion Sensitivity to Static Discharge: Not sensitive.

NFPA RATING



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

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. 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). Spills may be slippery.

PROTECTIVE EQUIPMENT:

Small Spills: For incidental spills (e.g., 1 vial), 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 airborne mists or sprays 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.**

6. ACCIDENTAL RELEASE MEASURES (Continued)

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 mists or sprays 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

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. Use non-sparking tools. 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.

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

CONDITIONS FOR SAFE STORAGE: Containers of this product must be properly labeled. Store between 36°-86°F (2°-30°C). Do not freeze. Under recommended storage conditions, a normal darkening of color may occur. Such darkening is characteristic of sugar solutions and does not affect therapeutic action. Prolonged exposure to temperatures above 86°F (30°C) or to direct light may cause extreme darkening and turbidity which may be pharmaceutically objectionable. If this condition develops, do not use. Prolonged exposure to freezing temperatures may cause change to a semi-solid, too viscous to pour. Viscosity will return to normal upon warming to room temperature. Material should be stored in secondary containers or in a diked area, as appropriate. Store away from incompatible materials (see Section 10, Stability and Reactivity). 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. Material should be stored in secondary containers or in a diked area, as appropriate. Store containers away from incompatible chemicals (see Section 10, Stability and Reactivity). Empty containers may contain residual liquid or vapors which are flammable; therefore, empty containers should be handled with care.

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.

Occupational/Workplace Exposure Limits/Guidelines:

CHEMICAL NAME	CAS #	EXPOSURE LIMITS IN AIR							
		ACGIH-TLVs		OSHA-PELs		NIOSH-RELs		NIOSH	OTHER
		TWA ppm	STEL ppm	TWA ppm	STEL ppm	TWA ppm	STEL ppm	IDLH ppm	ppm
Lactulose	4618-18-2	NE	NE	NE	NE	NE	NE	NE	NE
Fructose	57-48-7	NE	NE	NE	NE	NE	NE	NE	NE
Galactose	59-23-4	NE	NE	NE	NE	NE	NE	NE	NE
Lactose	6342-3	NE	NE	NE	NE	NE	NE	NE	NE
Water	7732-18-5	NE	NE	NE	NE	NE	NE	NE	NE

NE = Not Established

International Occupational Exposure Limits: Currently no additional international exposure limits are in place for components of this product. Limits may be added; consult appropriate authorities for currency.

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.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

PERSONAL PROTECTIVE EQUIPMENT (continued):

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

FORM: Aqueous solution.
COLOR: Natural.
MOLECULAR WEIGHT: Mixture.
MOLECULAR FORMULA: Mixture.
ODOR: Faint odor.
ODOR THRESHOLD: Not applicable.
BOILING POINT: Similar to water.
FREEZING/MELTING POINT Similar to water.
EVAPORATION RATE (nBuAc = 1): Not established.
SOLUBILITY IN WATER: Partially soluble.
VAPOR PRESSURE (air = 1): Not available.
SPECIFIC GRAVITY (water = 1): Not available.
pH: Not established.
VAPOR DENSITY: Not available.
COEFFICIENT WATER/OIL DISTRIBUTION: Not established.
VISCOSITY: Not available.

HOW TO DETECT THIS SUBSTANCE (identification/warning properties): There are no good warning characteristics of this product that may act as a distinguishing characteristic to identify it in event of an accidental release.

10. STABILITY and REACTIVITY

CHEMICAL STABILITY: This product is stable.

DECOMPOSITION PRODUCTS: **Combustion:** If exposed to extremely high temperatures, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon, potassium and nitrogen oxides). **Hydrolysis:** None known.

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: This product is generally compatible with other common materials in a medical facility.

POSSIBILITY OF HAZARDOUS REACTIONS OR POLYMERIZATION: Will not occur.

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 medical employees using this product in an occupational setting. The following paragraphs describe the symptoms of exposure by route of exposure.

Inhalation: If vapors, mists, or sprays of the product are inhaled, they may cause coughing and temporary bronchial irritation. No other effects are known by this route of exposure.

Contact with Skin or Eyes: Prolonged skin contact may cause dermatitis (dry, red, cracked skin). Contact of this product with the eyes may cause irritation, redness, and tearing.

Skin Absorption: No information available on possible effects from this route of exposure.

Ingestion: ingestion caused by poor hygiene practices may cause adverse symptoms. Very large doses of Lactose may cause abdominal pain and diarrhea. Some people are lactose intolerant (have reduced ability to digest lactose); these people may experience the same symptoms at smaller doses. It is unlikely that an accidental occupational ingestion would cause an intolerance reaction.

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.

OTHER POTENTIAL HEALTH EFFECTS-Therapeutic Doses: In therapeutic use, Lactulose may produce gaseous distention with flatulence or belching and abdominal discomfort such as cramping in about 20% of patients. Excessive dosage can lead to diarrhea with potential complications such as loss of fluids, hypokalemia, and hypernatremia. Nausea and vomiting have been reported.

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

HEALTH HAZARD	(BLUE)	1
FLAMMABILITY HAZARD	(RED)	0
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: The primary health effects that may be experienced by medical personnel exposed to this product is mild irritation of contaminated eyes.

Chronic: Repeated skin contact may cause dermatitis (dry, red skin).

11. TOXICOLOGICAL INFORMATION (Continued)

TARGET ORGANS:

Acute: *Industrial Exposure*: Eyes, respiratory system. *Therapeutic Doses*: Gastrointestinal upset.

Chronic: *Industrial Exposure*: None. *Therapeutic Doses*: As described under 'Other Potential Health Effects'.

IRRITANCY OF PRODUCT: This product may irritate contaminated eyes, or may cause irritation if inhaled.

SENSITIZATION OF PRODUCT: No sensitization effects are known.

TOXICITY DATA: The following toxicity data are available for the active ingredients. Additional data are available for the excipient components of this product, but are not presented in this SDS. Contact Actavis for more information.

LACTULOSE:

TDLo (Unreported-Woman) 40 mg/kg/3 days: Nutritional and Gross Metabolic: changes in sodium

LD_{50} (Oral-Rat) 18,160 mg/kg

LD_{50} (Oral-Mouse) 31 gm/kg: Reproductive: Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated); Gastrointestinal: hypermotility, diarrhea; Nutritional and Gross Metabolic: body temperature decrease

LD_{50} (Intraperitoneal-Rat) 16 gm/kg

LD_{50} (Intraperitoneal-Mouse) 15,800 mg/kg: Lungs, Thorax, or Respiration: dyspnea; Nutritional and Gross Metabolic: dehydration, body temperature decrease

LD_{50} (Subcutaneous-Rat) 33,500 mg/kg: Lungs, Thorax, or Respiration: dyspnea; Skin and Appendages: dermatitis, other (after systemic exposure); Nutritional and Gross Metabolic: body temperature decrease

LD_{50} (Subcutaneous-Mouse) 29,600 mg/kg: Lungs, Thorax, or Respiration: dyspnea; Skin and Appendages: dermatitis, other (after systemic exposure); Nutritional and Gross Metabolic: dehydration

LD_{50} (Intravenous-Rat) 13,500 mg/kg: Lungs, Thorax, or Respiration: dyspnea; Nutritional and Gross Metabolic: dehydration, body temperature decrease

LD_{50} (Intravenous-Mouse) 9960 mg/kg: Lungs, Thorax, or Respiration: dyspnea; Nutritional and Gross Metabolic: dehydration, body temperature decrease

LD (Oral-Dog) > 12 gm/kg: Gastrointestinal: nausea or vomiting

LDLo (Oral-Rabbit) 24 gm/kg: Behavioral: muscle weakness, ataxia; Lungs, Thorax, or Respiration: respiratory depression

TDLo (Oral-Rat) 648 gm/kg/6 weeks-intermittent: Kidney/Ureter/Bladder: changes in tubules (including acute renal failure, acute tubular necrosis), changes in bladder weight; Nutritional and Gross Metabolic: weight loss or decreased weight gain

TDLo (Oral-Rat) 2592 gm/kg/24 weeks-intermittent: Endocrine: changes in adrenal weight; Blood: normocytic anemia; Related to Chronic Data: death

TDLo (Oral-Dog) 864 gm/kg/12 weeks-intermittent: Gastrointestinal: ulceration or bleeding from small intestine; Nutritional and Gross Metabolic: dehydration; Related to Chronic Data: death

FRUCTOSE:

LD_{50} (Intravenous-Rabbit) 15 gm/kg

TDLo (Oral-Rat) 4 gm/kg

TDLo (Oral-Rat) 4 gm/kg: Kidney/Ureter/Bladder: other changes in urine composition

TDLo (Oral-Rat) 119 mg/kg/14 days-intermittent: Blood: other changes; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: true cholinesterase; Related to Chronic Data: death

TDLo (Oral-Rat) 140 gm/kg/2 weeks-intermittent: Liver: other changes; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol); Biochemical: Metabolism (Intermediary): lipids including transport

TDLo (Oral-Rat) 70 gm/kg/1 week-continuous: Behavioral: fluid intake

TDLo (Oral-Rat) 70 gm/kg/3 weeks-continuous: Behavioral: food intake (animal); Cardiac: pulse rate increase, without fall in BP; Vascular: BP elevation not characterized in autonomic section

TDLo (Oral-Rat) 42 gm/kg/1 week-continuous: Vascular: BP elevation not characterized in autonomic section

TDLo (Oral-Rat) 168 gm/kg/4 weeks-continuous: Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: transaminases; Endocrine: other changes

TDLo (Oral-Rat) 700,000 mg/kg/35 days-continuous: Gastrointestinal: other changes; Liver: changes in liver weight

TDLo (Oral-Rat) 2160 gm/kg/60 days-intermittent: Endocrine: hyperglycemia; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol); Biochemical: Metabolism (Intermediary): lipids including transport

TDLo (Oral-Rat) 605.25 gm/kg/8 weeks-continuous: Vascular: BP elevation not characterized in autonomic section; Endocrine: other changes; Biochemical: Metabolism (Intermediary): lipids including transport

TDLo (Oral-Rat) 140 gm/kg/2 weeks-continuous: Cardiac: cardiac output, other changes

TDLo (Oral-Rat) 700 gm/kg/8 weeks-continuous: Vascular: BP elevation not characterized in autonomic section, contraction (isolated tissues), relaxation (isolated tissues)

TDLo (Oral-Rat) 140 gm/kg/2 weeks-continuous: Vascular: BP elevation not characterized in autonomic section; Endocrine: other changes; Biochemical: Metabolism (Intermediary): lipids including transport

TDLo (Oral-Rat) 2376 gm/kg/60 days-intermittent: Endocrine: hyperglycemia, other changes; Biochemical: Metabolism (Intermediary): lipids including transport

TDLo (Oral-Rat) 560 gm/kg/8 weeks-continuous: Kidney/Ureter/Bladder: renal function tests depressed; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: xanthine oxidases, Metabolism (Intermediary): xanthine, purine or nucleotides including urate

TDLo (Oral-Rat) 840 gm/kg/12 weeks-continuous: Vascular: BP elevation not characterized in autonomic section; Endocrine: hyperglycemia, other changes

TDLo (Oral-Rat) 257.6 gm/kg/14 days-continuous: Liver: hepatitis (hepatocellular necrosis), diffuse, changes in liver weight; Biochemical: Metabolism (Intermediary): lipids including transport

GALACTOSE:

ICLo (*In vitro*-Mouse-Other Normal Tissue) 80 µmol/L/5 days: *In Vitro* Toxicity Studies: other assays

TDLo (Oral-Rat) 294 gm/kg/14 days-continuous: Sense Organs and Special Senses (Eye): effect, not otherwise specified

TDLo (Oral-Rat) 4860 gm/kg/23 weeks-continuous: Sense Organs and Special Senses (Eye): effect, not otherwise specified

GALACTOSE (continued):

TDLo (Oral-Rat) 190 gm/kg/19 days-intermittent: Reproductive: Maternal Effects: ovaries, fallopian tubes

TDLo (Oral-Rat) 209.642 gm/kg/37 days-continuous: Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: other oxidoreductases; Metabolism (Intermediary): lipids including transport

TDLo (Oral-Rat) 240 gm/kg: female 11-22 day(s) after conception: Reproductive: Effects on Embryo or Fetus: fetotoxicity (except death, e.g., stunted fetus)

TDLo (Oral-Rat) 188 gm/kg: female 8-10 day(s) after conception: Reproductive: Specific Developmental Abnormalities: eye/ear; Fertility: post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants)

TDLo (Oral-Rat) 440 gm/kg: female 1-22 day(s) after conception: Reproductive: Effects on Embryo or Fetus: fetotoxicity (except death, e.g., stunted fetus); Effects on Newborn: growth statistics (e.g. %, reduced weight gain)

TDLo (Oral-Rat) 475 gm/kg: female 3-22 day(s) after conception: Reproductive: Effects on Newborn: other postnatal measures or effects

TDLo (Oral-Rat) 1000 gm/kg: female 3-22 day(s) after conception lactating female 21 day(s) post-birth: Reproductive: Effects on Newborn: germ cell effects (in offspring)

TDLo (Oral-Rat) 209.642 gm/kg: female 7 day(s) after conception: 21 day(s) post-birth: Reproductive: Specific Developmental Abnormalities: eye/ear, other developmental abnormalities

TDLo (Oral-Mouse) 1260 gm/kg: female 1-21 day(s) after conception: Reproductive: Fertility: abortion; Effects on Newborn: viability index (e.g., # alive at day 4 per # born alive)

TDLo (Oral-Mouse) 630 gm/kg: female 1-21 day(s) after conception: Reproductive: Specific Developmental Abnormalities: eye/ear

TDLo (Oral-Mouse) 16,500 mg/kg: female 8-12 day(s) after conception: Reproductive: Effects on Newborn: live birth index (measured after birth)

TDLo (Oral-Mouse) 840 gm/kg: female 14 day(s) pre-mating: Reproductive: Maternal Effects: ovaries, fallopian tubes; Fertility: other measures of fertility

TDLo (Intraperitoneal-Mouse) 5640 mg/kg/47 days-intermittent: Behavioral: changes in psychophysiological tests; Endocrine: changes in spleen weight

TDLo (Intraperitoneal-Mouse) 5600 mg/kg/8 weeks-intermittent: Brain and Coverings: other degenerative changes; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: other oxidoreductases, Metabolism (Intermediary): effect on inflammation or mediation of inflammation

TDLo (Intraperitoneal-Mouse) 21,000 mg/kg/42 days-intermittent: Liver: other changes; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: catalyses, other oxidoreductases

TDLo (Subcutaneous-Mouse) 5.04 gm/kg/6 weeks-intermittent: Behavioral: alteration of classical conditioning, changes in motor activity (specific assay)

TDLo (Subcutaneous-Mouse) 2800 mg/kg/10 weeks-intermittent: Behavioral: changes in motor activity (specific assay), alteration of operant conditioning; Immunological Including Allergic: decrease in cellular immune response

TDLo (Subcutaneous-Mouse) 28,000 mg/kg/8 weeks-intermittent: Liver: other changes; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: multiple enzyme effects; Metabolism (Intermediary): effect on inflammation or mediation of inflammation

TDLo (Subcutaneous-Mouse) 6300 mg/kg/6 weeks-intermittent: Brain and Coverings: other degenerative changes; Behavioral: alteration of classical conditioning, Enzyme inhibition, induction, or change in blood or tissue levels: dehydrogenases

TDLo (Subcutaneous-Mouse) 6300 mg/kg/6 weeks-intermittent: Brain and Coverings: other degenerative changes; Behavioral: alteration of classical conditioning, Enzyme inhibition, induction, or change in blood or tissue levels: other oxidoreductases

TDLo (Subcutaneous-Mouse) 28,000 mg/kg/8 weeks-intermittent: Liver: other changes; Biochemical: Metabolism (Intermediary): lipids including transport, effect on inflammation or mediation of inflammation

TDLo (Subcutaneous-Mouse) 4200 mg/kg/6 weeks-intermittent: Brain and Coverings: other degenerative changes; Behavioral: alteration of classical conditioning, Metabolism (Intermediary): effect on mitochondrial function

TDLo (Subcutaneous-Mouse) 28,000 mg/kg/8 weeks-intermittent: Liver: other changes; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: other oxidoreductases, other transferases

TDLo (Subcutaneous-Mouse) 28,000 mg/kg/8 weeks-intermittent: Kidney/Ureter/Bladder: changes in both tubules and glomeruli, renal function tests depressed; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: other oxidoreductases

TDLo (Subcutaneous-Mouse) 6300 mg/kg/6 weeks-intermittent: Brain and Coverings: other degenerative changes; Behavioral: alteration of classical conditioning; Liver: other changes

TDLo (Subcutaneous-Mouse) 7350 mg/kg/7 weeks-intermittent: Brain and Coverings: other degenerative changes; Behavioral: alteration of classical conditioning; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: other oxidoreductases

LACTOSE ANHYDROUS:

LD_{50} (Oral-Rat) > 10 gm/kg

LD_{50} (Subcutaneous-Rat) > 5 gm/kg

LD_{50} (Intraperitoneal-Rat) > 10 gm/kg

IC_{50} (*In vitro*-Rat Lung) > 10 mmol/L/24 hours: In Vitro Toxicity Studies: cell counting

LDLo (Intravenous-Dog) 1500 mg/kg

TDLo (Oral-Rat) 4452 gm/kg/53 weeks-continuous: Gastrointestinal: other changes; Nutritional and Gross Metabolic: weight loss or decreased weight gain; Related to Chronic Data: changes in testicular weight

11. TOXICOLOGICAL INFORMATION (Continued)

TOXICITY DATA (continued):

LACTOSE ANHYDROUS (continued):

TDLo (Oral-Rat) 420 gm/kg/4 weeks-continuous: Gastrointestinal: hypermotility, diarrhea, other changes; Nutritional and Gross Metabolic: weight loss or decreased weight gain

TDLo (Oral-Rat) 375 mg/kg: female 4-18 day(s) after conception: Reproductive: Specific Developmental Abnormalities: musculoskeletal system

LACTOSE ANHYDROUS (continued):

TDLo (Oral-Dog) 41 gm/kg/26 weeks-continuous: Cardiac: changes in heart weight; Blood: pigmented or nucleated red blood cells, changes in erythrocyte (RBC) count

TDLo (Subcutaneous-Mouse) 1000 gm/kg/29 weeks-continuous: Tumorigenic: equivocal tumorigenic agent by RTECS criteria, tumors at site of application

OTHER ANIMAL TOXICITY DATA: The acute oral LD_{50} of the drug is 48.8 mL/kg in mice and greater than 30 mL/kg in rats.

CARCINOGENIC POTENTIAL OF COMPONENTS: Administration of Lactulose solution in the diet of mice for 18 months in concentrations of 3 and 10 percent (v/w) did not produce any evidence of carcinogenicity. there are no known human data on long-term potential for carcinogenicity.

The components of this product are 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 this product in pregnant women. This product is rated 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: There are no known human data on long-term potential for mutagenicity.

Embryotoxicity/Teratogenicity: In studies of mice, rats, and rabbits, doses of Lactulose solution up to 6 or 12 mL/kg/day produced no deleterious effects on breeding, conception, or parturition.

Reproductive Toxicity: There are no known human data on long-term potential for impairment of fertility. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Lactulose solution is administered to a nursing woman.

ACGIH BIOLOGICAL EXPOSURE INDICES (BEIs): Currently, no ACGIH Biological Exposure Indices (BEIs) have been determined for any component of this product.

12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

MOBILITY: This product has not been tested for mobility in soil; it is expected to be somewhat mobile due to its composition.

PERSISTENCE AND BIODEGRADABILITY: This product has not been tested for persistence or biodegradability. It is expected that the components will slowly degrade in the environment and form a variety of organic materials; however, no specific information is known.

BIO-ACCUMULATION POTENTIAL: This product has not been tested for bioaccumulation potential.

ECOTOXICITY: This product may be harmful to contaminated plant and animal life, especially in large quantities. All releases to terrestrial, atmospheric and aquatic environments should be avoided. No specific data is available for this product.

OTHER ADVERSE EFFECTS: This product does not contain any component with known ozone depletion potential.

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.

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 REGULATIONS: This product is not classified as dangerous goods, per U.S. DOT regulations, under 49 CFR 172.101.

TRANSPORT CANADA, TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: 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.

14. TRANSPORTATION INFORMATION (Continued)

INTERNATIONAL MARITIME ORGANIZATION (IMO) DESIGNATION: This product is not classified as Dangerous Goods by the International Maritime Organization.

EUROPEAN AGREEMENT CONCERNING THE INTERNATIONAL CARRIAGE OF DANGEROUS GOODS BY ROAD (ADR): 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: The active ingredient of this product can cause harm to aquatic organisms, according to the criteria of the UN Model Regulations (as reflected in the IMDG Code, ADR, RID, and ADN); the active ingredient is not a listed marine pollutant, under the to the IMDG Code and is not listed in Annex III under MARPOL 73/78.

15. REGULATORY INFORMATION

ADDITIONAL 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.

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

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

ANSI LABELING (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): CAUTION! MAY CAUSE EYE OR RESPIRATORY IRRITATION. ACCIDENTAL INGESTION MAY CAUSE STOMACH PAIN AND DIARRHEA. Do not taste or swallow. Avoid contact with skin, eyes, and clothing. Avoid breathing vapors. Keep container tightly closed. Use only with adequate ventilation. 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 inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. If swallowed, do NOT induce vomiting. If vomiting occurs, have person lean forward. Call physician or poison control center immediately. Never give anything by mouth to an unconscious person. IN CASE OF FIRE: Use water fog, dry chemical, CO_2, or "alcohol" foam. IN CASE OF SPILL: Wipe up spilled product. Place residue 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.

CLASSIFICATION OF COMPONENTS:

CLP Regulation (EC) 1272/2008

All Components: An official classification for these substances has not been published in the CLP 1272: 2008 and a self-classification is not 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: New.

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 compound. To the best of Actavis, 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 compound. If this compound 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.

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