Depomed™
Enhancing Pharmaceuticals

Material Safety Data Sheet

Product Name: Zipsor® (Diclofenac Potassium) Liquid Filled Capsules
Effective Date: 04/29/2013
MSDS #: 012

Depomed, Inc encourages and expects you to read and understand the entire MSDS, as there is important information throughout the document. Depomed expects you to follow the precautions identified in this document unless your conditions would necessitate other appropriate methods or actions.

Section 1: Product and Company Identification

Product Identification

Product Name:	Zipsor® (Diclofenac Potassium) Liquid Filled Capsules
Active Ingredient	Diclofenac Potassium
Chemical Family	Non-Steroidal Anti-Inflammatory (NSAID)
Chemical Name	1-(aminomethyl)-Cyclohexaneacetic acid,
Formula	Mixture

Company Identification

Depomed, Inc.
7999 Gateway Blvd, Suite 300
Newark, CA 94560
Phone Number: (510)744-8000
Fax Number: (510)744-8001

Section 2: Composition/Information on Ingredients

Ingredient Name	CAS Number	Exposure Limits
Zipsor		
Diclofenac Potassium	15307-81-0	Not established
Polysorbate	80 9005-65-6	none listed OSHA
Sorbitol	50-70-4	none listed OSHA
Povidone	9003-39-8	none listed OSHA
Glycerin	56-81-5	15 mg/m3 TWA
Polyethylene Glycol	25322-68-3	100 mg/m3 STEL

Amount of each ingredient in the Zipsor Capsule is withheld as a trade secret.

Gelatin Capsule		
Gelatin	9000-70-8	none listed OSHA
Glycerin	56-81-5	15 mg/m3 TWA

Black Colorant	NA	Not Available
Sorbitol	50-70-4	none listed OSHA
Water	7732-18-5	none listed OSHA

Section 3: Hazard Identification

Appearance: translucent, pale yellow, liquid-filled capsules printed with "X592" in black ink.

Odor: None

Hazards of product Product poses little or no hazard if spilled

Potential Health Effects

Route(s) of Entry: Skin Contact, Eye Contact, and Ingestion

Human Effects and Symptoms of Overexposure

Skin Hazards

Direct contact with damaged gelcaps may cause contact dermatitis, itching, rash, dry skin, and scaling, especially in sensitive individuals. Although Diclofenac Potassium can be absorbed through the skin, there are no reports of systemic effects by this route..

Eye Hazards

Direct contact with damaged gelcaps may irritate the eyes and cause redness and tearing.

Inhalation Hazards

No hazard is expected from normal clinical use or administration. Inhalation of aerosolized liquid from damaged gelcaps may irritate the respiratory system and cause coughing and sneezing.

Ingestion Hazards

No hazard is expected from normal clinical use or administration. Oral overdose can cause lethargy, drowsiness, nausea, vomiting, epigastric pain, gastrointestinal bleeding, high blood pressure, acute renal failure, respiratory depression, and coma. See "Therapeutic

Side Effects" in Section 11 (Toxicological Information) for information on effects by ingestion of therapeutic doses.

Medical Conditions Aggravated by Exposure Hypersensitivity to other NSAIDS and aspirin, gastrointestinal problems, cardiovascular problems.

Exposure: Hypersensitivity to any ingredient in Zipsor (Diclofenac Potassium)

Cross Sensitivity: None known

Pregnancy: There are no adequate and well-controlled studies of Zipsor Liquid Filled Capsules (25 mg) in pregnant women.

Pregnancy Category: C prior to 30 weeks gestation; Category D starting 30 weeks gestation.

Starting at 30 weeks gestation, Zipsor, and other NSAIDs, should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Zipsor can cause fetal harm when administered to a pregnant woman starting at 30 weeks gestation. If this drug is used during this time period in pregnancy, the patient should be apprised of the potential hazard to a fetus. There are no adequate and well-controlled studies in pregnant women. Prior to 30 weeks gestation, Zipsor should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Carcinogenic Active Ingredients

NTP:	Not listed
IARC:	Not listed
OSHA	Not listed
ACGIH	Not listed
EPS	Not listed
MAK	Not listed
NIOSH	Not listed

Section 4: First Aid Measures

Overdose: Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose (5 to 10 times the usual dose). Forced diuresis, alkalinization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding..

Eye: Flush with running water for 20 minutes holding eyelids open. Seek medical attention if adverse effect occurs.

Skin: Wash contaminated area with soap and water. Seek medical attention if adverse effect occurs.

Inhalation: No specific treatment is necessary since this product is not likely to be hazardous by inhalation. Seek medical attention if adverse effect occurs.

Ingestion: Get medical attention immediately overdoes is suspected or if person has adverse symptoms.

Notes to Physicians: Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Administration of activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose (5 to 10 times the usual dose). Forced diuresis, alkalinization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

Section 5: Fire Fighting Measures

Suitable Extinguishing Media:

Use carbon dioxide, dry chemical, or alcohol type foam extinguishers or water fog.

Special Exposure Hazards:

This product may decompose and produce irritating fumes and toxic gases when involved in a fire.

Special Protective Equipment for Firefighters:

Self-contained positive pressure respiratory equipment and full protective clothing.

Decomposition Products:

Thermal decomposition may result in the emission of carbon oxides, nitrogen oxides, and potassium oxides.

NFPA Ratings: Health = 1, Flammability = 1, Instability = 0, Special Hazard = None

Section 6: Accidental Release Measures

Spill Procedure:

Using appropriate protective equipment, wipe up and containerize spilled material. Avoid generation of mists or sprays during cleanup. Ignition sources should be identified and eliminated prior to cleanup beginning. Avoid contamination of sewers and waterways. Dispose of spilled material according to local regulations.

Section 7: Handling and Storage

Storage Temperature: Controlled Room Temperature: 25° C (77° F); excursions permitted to 15-30° C (59-86° F)

Shelf Life: See dating on product

Special Sensitivity: Protect from moisture.

Handling/Storage Precautions:

Keep this and all drugs out of the reach of children. Store in a dry place away from excessive heat. As this product must be prescribed by a physician, observe handling and storage requirements in compliance with Federal Drug Administration regulations.

Section 8: Exposure Controls/Personal Protection

Personal Protection Equipment

Eye Protection:	Not required under normal conditions of therapeutic administration and use.
Skin Protection:	Not required under normal conditions of therapeutic administration and use.
Ventilation:	Not required under normal conditions of therapeutic administration and use.
Respiratory:	Not required under normal conditions of therapeutic administration and use.

Section 9: Physical and Chemical Properties

Physical Form:	Soft gelatin capsule
Appearance:	translucent, pale yellow, liquid-filled capsules printed with "X592" in black ink. "
Color:	pale yellow
Molecular weight	Mixture
Molecular formula	Mixture
Odor:	None
Boiling Point:	Not Applicable
Melting/Freezing Point:	Not Applicable
Specific Gravity:	Not Established
Bulk Density:	Not Established
Vapor Pressure:	Not Applicable
Water Solubility	Slightly Soluble

Section 10: Stability and Reactivity

Stability	Stable under normal temperature and pressure
Hazardous Polymerization:	None
Substances to Avoid:	May react with strong oxidizing agents (e.g., peroxides, permanganates, nitric acid, etc.).
Conditions to Avoid:	Protect form light. Avoid extreme heat.

Decomposition Products: Thermal decomposition may result in the emission of carbon oxides, nitrogen oxides, and potassium oxides.

Section 11: Toxicological Information

Therapeutic Side Effects: Individuals sensitive to Diclofenac Potassium, other NSAIDS, aspirin, or any other ingredient in this product may have an allergic reaction upon ingestion of this product. The most frequently reported adverse effects include abdominal pain, constipation, diarrhea, indigestion, nausea, vomiting, dizziness, headaches, sleepiness, itching, increased sweating.

Other Target Organ Effects: NSAIDs can affect the body as a whole (fever, infection, sepsis). Cardiovascular system (congestive heart failure, heart attack, stroke, low blood pressure, rapid heartbeat, brief loss of consciousness). Digestive system (dry mouth, esophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, inflamed tongue, vomiting blood, hepatitis, jaundice). Hemic and lymphatic system (bruising; eosinophilia; leukopenia; black, tarry, bloody stools; purple or brownish-red spots on the skin or mucous membranes; rectal bleeding; stomatitis; thrombocytopenia). Metabolic and nutritional (weight changes). Nervous system (anxiety; weakness; confusion; depression; dream abnormalities drowsiness; insomnia; fatigue; nervousness; burning, prickling, itching, or tingling skin; sleepiness; tremors; vertigo). Respiratory system (asthma, difficulty breathing). Skin and appendages (hair loss, photosensitivity, increased sweating). Special senses (blurred vision). Urogenital system (cystitis, difficult or painful urination, blood in the urine, interstitial nephritis, oliguria/polyuria, abnormal amount of protein in the urine, renal failure).

Medical Conditions Aggravated By Exposure: Hypersensitivity to other NSAIDS and aspirin, gastrointestinal problems, cardiovascular problems.

Drug Interactions: For information on possible interactions with other drugs during therapeutic use, refer to Product Prescribing Information Sheet.

Human Data: There are no data for Diclofenac Potassium. The following data are for the Anhydrous Diclofenac.

DICLOFENAC:

TDLo (Oral-Man) 29 mg/kg: Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol)
TDLo (Oral-Human) 6 mg/kg: Blood: change in clotting factors
TDLo (Oral-Human) 10 mg/kg/10 days-intermittent: Skin and Appendages: dermatitis, allergic (after systemic exposure) Immunological Including; Allergic: hypersensitivity delayed
TDLo (Skin-Human) 6.4 mg/kg/30 days-intermittent: Skin and Appendages: dermatitis, allergic

(after systemic exposure), dermatitis, irritative (after systemic exposure)
TDLo (Intramuscular-Man) 1070 µg/kg: Skin and Appendages: dermatitis, other (after systemic exposure)
TDLo (Intramuscular-Man) 5.4 mg/kg/5 days-intermittent: Gastrointestinal: ulceration or bleeding from stomach; Blood: other hemolysis with or without anemia; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: dehydrogenases
TDLo (Rectal-Human) 0.65 mg/kg: Blood: hemorrhage
TDLo (Multiple Routes-Human) 4.2 mg/kg/2 days-intermittent: Behavioral: analgesia, Metabolism
(Intermediary): effect on inflammation or mediation of inflammation
TDLo (Intravenous-Human) 0.96 mg/kg: Skin and Appendages: dermatitis, other (after systemic exposure)
TDLo (Unreported-Human) 1.07 mg/kg: Behavioral: analgesia

Eye Irritation: Direct contact with damaged gelcaps may irritate the eyes and cause redness and tearing.

Skin Irritation/Sensitization: Direct contact with damaged gelcaps may cause contact dermatitis, itching, rash, dry skin, and scaling, especially in sensitive individuals.

Oral Toxicity: Oral overdose can cause lethargy, drowsiness, nausea, vomiting, epigastric pain, gastrointestinal bleeding, anemia, adverse cardiovascular effects, high blood pressure, acute renal failure, respiratory depression, adverse effects on liver and kidneys (including failure), life-threatening skin reactions, life-threatening allergic reactions, triggering of asthma, and coma. There are no data for Diclofenac Potassium. The following data are for the Anhydrous Diclofenac.

ANHYDROUS DICLOFENAC:
LD50 (Oral-Rat) 62,500 µg/kg
LD50 (Oral-LD50 (Oral-Mouse) 170 mg/kg
LD50 (Intraperitoneal-Mouse) 345 mg/kg

Dermal Toxicity: Although Diclofenac Potassium can be absorbed through the skin, there are no reports of systemic effects by this route.
Inhalation Toxicity: No well-controlled studies have been performed on product.

Subchronic: There are no data for Diclofenac Potassium. The following data are for the Anhydrous Diclofenac.

ANHYDROUS DICLOFENAC:
TDLo (Oral-Rat) 562.7 µg/kg: Behavioral: analgesia
TDLo (Oral-Rat) 50 mg/kg: Gastrointestinal: ulceration or bleeding from small intestine; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol)
TDLo (Oral-Rat) 0.05 mg/kg: Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation

TDLo (Oral-Rat) 5 mg/kg: Behavioral: analgesia; Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation
TDLo (Oral-Rat) 0.13 mg/kg: Nutritional and Gross Metabolic: body temperature decrease TDLo (Oral-Rat) 3 mg/kg: Gastrointestinal: ulceration or bleeding from stomach
TDLo (Oral-Rat) 30 mg/kg: Gastrointestinal: other changes
TDLo (Oral-Rat) 12 mg/kg/4 days-intermittent: Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation
TDLo (Oral-Rat) 250 mg/kg/5 days-intermittent: Gastrointestinal: ulceration or bleeding from small intestine, ulceration or bleeding from large intestine; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol)
TDLo (Oral-Rat) 34 mg/kg/17 days-intermittent: Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation
TDLo (Oral-Rat) 12 mg/kg/4 days-intermittent: Gastrointestinal: other changes
TDLo (Oral-Rat) 50 mg/kg/2 days-intermittent: Behavioral: somnolence (general depressed activity); Gastrointestinal: other changes; Related to Chronic Data: death
TDLo (Oral-Mouse) 0.8 mg/kg: Behavioral: analgesia
TDLo (Oral-Mouse) 0.95 mg/kg: Liver: other changes
TDLo (Oral-Mouse) 9.5 mg/kg: Liver: hepatitis (hepatocellular necrosis), zonal
TDLo (Oral-Mouse) 75 mg/kg/6 days-intermittent: Immunological Including Allergic: decrease in cellular immune response
TDLo (Oral-Mouse) 75 mg/kg/3 days-intermittent: Blood: other hemolysis with or without anemia, other changes, changes in erythrocyte (RBC) count
TDLo (Oral-Guinea Pig) 10 mg/kg: Lungs, Thorax, or Respiration: respiratory obstruction

Carcinogenicity: Long-term carcinogenicity studies in rats given diclofenac sodium up to 2
mg/kg/day (or 12 mg/m2/day, 0.2-fold an adult human daily dose of 100 mg/day) have revealed no significant increase in tumor incidence. A 2-year carcinogenicity study conducted in mice employing diclofenac sodium at doses up to 0.3 mg/kg/day (0.9 mg/m2/day, 0.014-fold an adult human daily dose of 100 mg/day) in males and 1 mg/kg/day (3 mg/m2/day, 0.04-fold an adult human daily dose of 100 mg/day) in females did not reveal any oncogenic potential.

Active ingredients:
ACGIH: Not listed
EPA: Not listed
IARC: Not listed
MAK: Not listed
NIOSH: Not listed

NTP: Not listed
OSHA: Not listed

Mutagenicity: Diclofenac sodium did not show mutagenic activity in *in vitro* point mutation assays in mammalian (mouse lymphoma) and microbial (yeast, Ames) test systems and was non-mutagenic in several mammalian *in vitro* and *in vivo* tests, including dominant lethal and male germinal epithelial chromosomal aberration studies in Chinese hamsters.

Reproductive Hazards: Starting at 30 weeks gestation, Zipsor, and other NSAIDs, should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Prior to 30 weeks gestation, Zipsor should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Diclofenac sodium administered to male and female rats at 4 mg/kg/day (24 mg/m2/day, 0.4-fold an adult human daily dose of 100 mg/day) did not affect fertility. There are no data for Diclofenac Potassium. The following data are for the Anhydrous Diclofenac.

ANHYDROUS DICLOFENAC:

TDLo (Oral-Mouse) 4 mg/kg: female 13 day(s) after conception: Reproductive: Specific Developmental Abnormalities: craniofacial (including nose and tongue)
TDLo (Oral-Rabbit) 75 mg/kg: female 9-11 day(s) after conception: Reproductive: Effects on Embryo or Fetus: fetotoxicity (except death, e.g., stunted fetus)

Section 12: Ecological Information

No data available for this product

Section 13: Disposal Considerations

Waste disposal Method: Disposal must be in accordance with applicable federal, state, and local laws and regulations. Dispose of any cleanup materials and waste residue according to all applicable laws and regulations.

Section 14: Transportation Information

Ground Regulations:

Proper Shipping Description:	Drugs, N.O.I., NMFC Item 60000
DOT Proper Shipping Name:	Not Applicable
DOT Hazard Class:	Not Applicable
DOT Identification Number:	Not Applicable

Packing Group:	Not Applicable

Ground Regulations:

Hazard Label:	Not Applicable
Package Weight Limits:	Not Applicable
Special Requirements:	Not Applicable
Exceptions:	Not Applicable
Non-Bulk Requirements:	Not Applicable
Bulk Requirements:	Not Applicable
Reportable Quantity (lb.):	Not Applicable
Stowage: Not Applicable	
Other Requirements:	Not Applicable

Air Regulations:

Proper Shipping Description:	Drugs, N.O.I., NMFC Item 60000
IATA Proper Shipping Name:	Not Applicable
IATA Hazard Class:	Not Applicable
IATA Identification Number:	Not Applicable
Packing Group:	Not Applicable
Hazard Label:	Not Applicable
Special Requirements:	Not Applicable
Max. wgt/pkg - Passgr. Aircraft:	Not Applicable
Max. wgt/pkg - Cargo Only Air:	Not Applicable

Section 15: Regulatory Information

Zipsor Liquid Filled Capsule (25 mg) is regulated under the Federal Food, Drug and Cosmetic Act of the United State of America.

OSHA (Occupational Safety & Health Administration): This Material Safety Data Sheet contains the information required by the Federal OSHA Hazard Communication Standard (29 CFR 1910.1200).

OSHA PSM (Process Safety Management): Not listed (29 CFR 1910.119, Appendix A).

NJ TCPA (Toxic Catastrophe Prevention Act): This product contains NONE of the substances subject to the reporting requirements of Section N.J.A.C. 7:31 of this act.
TSCA (Toxic Substance Control Act): Not applicable
CERCLA (Comprehensive Response Compensation & Liability Act): Not listed
SARA Title III (Superfund Amendments & Reauthorization Act):

Section 302 Extremely Hazardous Substances: Not listed
Section 311/312 Hazard Categories: Not applicable
Section 313 Reportable Ingredients: Not listed

RCRA (Resource Conservation & Recovery Act): Not listed

Other State Regulatory Information:
New Jersey: NJ RTK Threshold Planning Quantity = 10,000 lb.

California Proposition 65: The following statement is made in order to comply with the California Safe Drinking Water and Toxic Enforcement Act of 1986. *This product contains no chemicals known to the State of California to cause cancer or reproductive toxicity.*

Canada:
WHMIS Ingredient Disclosure List: Not listed
WHMIS Classification: D2A: Other Toxic Effects: Acute Effects/Chronic Effects

Section 16: Other Information

Reason for Issue: New (06/19/2012)
Supersedes Date: Not applicable

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