SAFETY DATA SHEET

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

Product Identifier

Material Name: Diclofenac Sodium and Misoprostol Tablets (Greenstone LLC)

Trade Name: Not applicable
Chemical Family: Mixture

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

Intended Use: Pharmaceutical product used as non-steroidal, anti-inflammatory drug (nsaid)

Details of the Supplier of the Safety Data Sheet

Greenstone LLC
100 Route 206 North
Peapack, NJ 07977
800-435-7095

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Acute Oral Toxicity: Category 4
Skin Corrosion/Irritation: Category 2
Serious Eye Damage/Eye Irritation: Category 2
Reproductive Toxicity: Category 1B

EU Classification:

EU Indication of danger: Harmful
Toxic to Reproduction: Category 2

EU Risk Phrases:

R22 - Harmful if swallowed.
R61 - May cause harm to the unborn child.

Label Elements

Signal Word: Danger
Hazard Statements: H315 - Causes skin irritation
H319 - Causes serious eye irritation
H302 - Harmful if swallowed
H360D - May damage the unborn child

Other Hazards No data available

Australian Hazard Classification (NOHSC): Hazardous Substance. Non-Dangerous Goods.

Note: This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	GHS Classification	%
Diclofenac Sodium	15307-79-6	239-346-4	T; R25; Xi,R36/38; Repr. Cat.2, R61; R52/53	Skin Irrit 2 (H315) Eye Irrit.2A (H319) Acute Tox.3 (H301) Repr.1B (H360D) Aquatic Acute 3 (H402) Aquatic Chronic 3 (H412)	8-15
Misoprostol	59122-46-2	Not Listed	T;R25 Repr.Cat.1;R60-61	Acute Tox. 3 (H301) Repr.1A (H360FD)	<1.0

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	GHS Classification	%
Methacrylic acid copolymer	25086-15-1	Not Listed	Not Listed	Not Listed	*
Triethyl Citrate	77-93-0	201-070-7	Not Listed	Not Listed	*

Additional Information: * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.
In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

For the full text of the R phrases and CLP/GHS abbreviations mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Description of First Aid Measures

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Most Important Symptoms and Effects, Both Acute and Delayed

Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.
Medical Conditions Aggravated by Exposure: None known

Indication of the Immediate Medical Attention and Special Treatment Needed
Notes to Physician: None

5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture
Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.

Fire / Explosion Hazards: Not applicable

Advice for Fire-Fighters
During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures
Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions
Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Methods and Material for Containment and Cleaning Up
Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling
Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

Conditions for Safe Storage, Including any Incompatibilities
Storage Conditions: Store as directed by product packaging.
Specific end use(s): Pharmaceutical drug product

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters
Refer to available public information for specific member state Occupational Exposure Limits.

Misoprostol
Manufacturer OEL: 0.7ug/m^3

Diclofenac Sodium
Manufacturer OEB: OEB2 (control exposure to the range of >100ug/m^3 to < 1000ug/m^3)

Exposure Controls
Engineering Controls: Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.
Personal Protective Equipment: Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

Hands: Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.
Eyes: Wear safety glasses or goggles if eye contact is possible.
Skin: Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.
Respiratory protection: If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Tablets	**Color:**	White
Odor:	No data available.	**Odor Threshold:**	No data available.
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

Solvent Solubility: No data available
Water Solubility: No data available
pH: No data available.
Melting/Freezing Point (°C): No data available
Boiling Point (°C): No data available.
Partition Coefficient: (Method, pH, Endpoint, Value)
Povidone
No data available
Corn Starch
No data available
Crospovidone
No data available
Talc (non-asbestiform)
No data available
Lactose Monohydrate
No data available
Silicon dioxide, colloidal NF
No data available
Magnesium stearate
No data available

9. PHYSICAL AND CHEMICAL PROPERTIES

Hydrogenated castor oil
No data available
Microcrystalline cellulose
No data available
Hydroxypropyl methylcellulose
No data available
Triethyl Citrate
No data available
Methacrylic acid copolymer
No data available
Diclofenac Sodium
Predicted Log P 4.51
Misoprostol
No data available

Decomposition Temperature (°C): No data available.

Evaporation Rate (Gram/s): No data available
Vapor Pressure (kPa): No data available
Vapor Density (g/ml): No data available
Relative Density: No data available
Viscosity: No data available

Flammablity:
- **Autoignition Temperature (Solid) (°C):** No data available
- **Flammability (Solids):** No data available
- **Flash Point (Liquid) (°C):** No data available
- **Upper Explosive Limits (Liquid) (% by Vol.):** No data available
- **Lower Explosive Limits (Liquid) (% by Vol.):** No data available

10. STABILITY AND REACTIVITY

Reactivity: No data available
Chemical Stability: Stable at normal conditions
Possibility of Hazardous Reactions
- **Oxidizing Properties:** No data available
- **Conditions to Avoid:** Fine particles (such as dust and mists) may fuel fires/explosions.
- **Incompatible Materials:** As a precautionary measure, keep away from strong oxidizers
- **Hazardous Decomposition Products:** No data available

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects
General Information: The information included in this section describes the potential hazards of the individual ingredients.
Short Term: May cause eye irritation May cause skin irritation. (based on components)
Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on blood spleen reproductive system gastrointestinal system Animal studies indicate that this material may cause adverse effects on the the developing fetus.

11. TOXICOLOGICAL INFORMATION

Known Clinical Effects: Clinical use has caused effects on the gastrointestinal system, including abdominal pain, nausea, vomiting, diarrhea, constipation, peptic ulcer, acid reflux, and gastrointestinal bleeding. Clinical use has resulted in liver effects. Symptoms may include jaundice, liver function test abnormalities, and hepatitis. Clinical use has caused effects on the nervous system, including drowsiness, anxiety, dizziness, visual disturbances. Serious allergic reactions, including anaphylaxis, have been reported. Clinical use of this drug has caused decreased red blood cell count (anemia), effects on blood forming organs. Drugs of this class may cause menstrual irregularities, cramps, pain, postmenopausal menstrual bleeding, miscarriage, uterine rupture, bleeding and death. Miscarriages have been seen in pregnant women taking this drug. Clinical use has caused effects on the cardiovascular system, including heart attack (myocardial infarction), stroke.

Acute Toxicity: (Species, Route, End Point, Dose)

Povidone
Rat Oral LD50 100 g/kg

Talc (non-asbestiform)
Rat Oral LD50 > 1600 mg/kg

Lactose Monohydrate
Rat Oral LD 50 29700 mg/kg

Magnesium stearate
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m^3

Microcrystalline cellulose
Rat Oral LD50 > 5000 mg/kg
Rabbit Dermal LD50 > 2000 mg/kg

Hydroxypropyl methylcellulose
Rat Oral LD50 > 10,000 mg/kg

Diclofenac Sodium
Rat Oral LD 50 53-77 mg/kg

Misoprostol
Rat Oral LD 50 81 mg/kg
Rat Inhalation LC 50 > 1.43mg/L
Mouse Oral LD 50 27mg/kg

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Microcrystalline cellulose
Skin Irritation Rabbit Non-irritating
Eye Irritation Rabbit Non-irritating

Diclofenac Sodium
Skin Irritation Positive

11. TOXICOLOGICAL INFORMATION

Eye Irritation Positive

Misoprostol
Skin Irritation Rabbit Mild

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Diclofenac Sodium
30 Day(s) Rat Oral 14 mg/kg LOAEL None identified
5 Week(s) Mouse Oral 9 mg/kg LOAEL Lungs, Spleen
26 Week(s) Rat Oral 50 mg/kg LOAEL Blood, Gastrointestinal system

Misoprostol
4 Week(s) Dog Intravenous 10 µg/kg/day LOEL Liver, Blood
13 Week(s) Rat Oral 120 µg/kg/day LOEL Gastrointestinal system
13 Week(s) Dog Oral 30 µg/kg/day LOEL Gastrointestinal system
1 Year(s) Rat Oral 160 µg/kg/day LOEL Gastrointestinal system
1 Year(s) Dog Oral 30 ug/kg/day LOEL Gastrointestinal system

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

Diclofenac Sodium
Embryo / Fetal Development Rat Oral 24 mg/kg LOAEL Maternal toxicity, Fetotoxicity
Embryo / Fetal Development Rat 1 mg/kg LOAEL Developmental toxicity
Embryo / Fetal Development Rat No route specified 20 mg/kg/day NOEL Not Teratogenic
Embryo / Fetal Development Rabbit No route specified 10 mg/kg/day NOEL Not Teratogenic

Misoprostol
Reproductive & Fertility Rat Oral 10 mg/kg/day LOAEL Fertility
Embryo / Fetal Development Rabbit Oral 1 mg/kg/day LOAEL Embryotoxicity
Embryo / Fetal Development Mouse Oral 30 mg/kg LOAEL Embryotoxicity
Embryo / Fetal Development Rabbit Oral 1 mg/kg/day NOAEL Not Teratogenic
Embryo / Fetal Development Rat Oral 10 mg/kg/day NOAEL Not Teratogenic

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Lactose Monohydrate
In Vitro Bacterial Mutagenicity (Ames) *Salmonella* , *E. coli* Negative

Diclofenac Sodium
Bacterial Mutagenicity (Ames) *Salmonella* Negative

Misoprostol
Bacterial Mutagenicity (Ames) *Salmonella* Negative
In Vitro Mouse Lymphoma Negative
Sister Chromatid Exchange Negative

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Diclofenac Sodium
Not specified Rat Oral 2 mg/kg/day NOEL Not carcinogenic

11. TOXICOLOGICAL INFORMATION

Misoprostol
21 Month(s) Mouse Oral 16 mg/kg/day NOAEL Not carcinogenic
24 Month(s) Rat Oral 2.4 mg/kg/day NOAEL Not carcinogenic

Carcinogen Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA. See below

Povidone
IARC: Group 3 (Not Classifiable)

Crospovidone
IARC: Group 3 (Not Classifiable)

Talc (non-asbestiform)
IARC: Group 3 (Not Classifiable)

Silicon dioxide, colloidal NF
IARC: Group 3 (Not Classifiable)

12. ECOLOGICAL INFORMATION

Environmental Overview: May have harmful effects on the aquatic environment. Releases to the environment should be avoided. This formulation has not been tested as a whole, the following apply to component substance(s):

Toxicity:

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Diclofenac Sodium
Oncorhynchus mykiss (Rainbow Trout) EC-50 96 Hours 130.6 mg/L
Daphnia magna (Water Flea) EC50 48 Hours 68 mg/L
Skeletonema costatum (Marine Diatom) ErC50 48 Hours 42 mg/L
Skeletonema costatum (Marine Diatom) EC-50 72 Hours 100 mg/L

Misoprostol
Daphnia LC-50 48 Hours > 932.5 mg/L
Oncorhynchus mykiss (Rainbow Trout) LC-50 72 Hours > 26.4 mg/L
Skeletonema costatum (Marine Diatom) ErC50 72 Hours > 104 mg/L
Skeletonema costatum (Marine Diatom) NOEC 26.5 mg/L

Aquatic Toxicity Comments: A greater than (>) symbol indicates that acute ecotoxicity was not observed at the maximum solubility. Since the substance is insoluble in aqueous solutions above this concentration, an acute ecotoxicity value (i.e. LC/EC50) is not achievable.

Persistence and Degradability:
Biodegradation: (Method, Inoculum, Biodeg Study, Result, Endpoint, Duration, Classification)
Diclofenac Sodium
Ready 55% After 28 Day(s) Not Ready

Bio-accumulative Potential:

Partition Coefficient: (Method, pH, Endpoint, Value)
Diclofenac Sodium
Predicted Log P 4.51

Mobility in Soil: No data available

13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

Canada - WHMIS: Classifications
WHMIS hazard class:
Class D, Division 1, Subdivision B
Class D, Division 2, Subdivision A

Diclofenac Sodium

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Australia (AICS):	Present
EU EINECS/ELINCS List	239-346-4

Misoprostol

CERCLA/SARA 313 Emission reporting	Not Listed

15. REGULATORY INFORMATION

California Proposition 65	developmental toxicity initial date 4/1/90
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	Not Listed

Methacrylic acid copolymer

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	Not Listed

Triethyl Citrate

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	201-070-7

16. OTHER INFORMATION

Text of R phrases and GHS Classification abbreviations mentioned in Section 3

Acute toxicity, oral-Cat.3; H301 - Toxic if swallowed
Skin corrosion/irritation-Cat.2; H315 - Causes skin irritation
Serious eye damage/eye irritation-Cat.2A; H319 - Causes serious eye irritation
Reproductive toxicity-Cat.1B; H360D - May damage the unborn child
Hazardous to the aquatic environment, acute toxicity-Cat.3; H402 - Harmful to aquatic life
Hazardous to the aquatic environment, chronic toxicity-Cat.3; H412 - Harmful to aquatic life with long lasting effects
Reproductive toxicity-Cat.1A; H360FD - May damage fertility. May damage the unborn child.

T - Toxic
Xi - Irritant
Toxic to Reproduction: Category 2
Toxic to reproduction: Category 1

R25 - Toxic if swallowed.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R36/38 - Irritating to eyes and skin.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Data Sources: The data contained in this SDS may have been gathered from confidential internal sources, raw material suppliers, or from the published literature.

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 7 - Handling and Storage. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 15 - Regulatory Information. Updated Section 11 - Toxicology Information. Updated Section 12 - Ecological Information. Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 16 - Other Information.

Revision date: 05-May-2015

Product Stewardship Hazard Communication
Prepared by: Global Environment, Health, and Safety Operations

It is believed that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without a warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time

End of Safety Data Sheet