MATERIAL SAFETY DATA SHEET

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

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-212-573-2222

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Contact E-Mail: pfizer-MSDS@pfizer.com

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
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+00 44 (0)1304 616161
Emergency telephone number:
International CHEMTREC (24 hours): +1-703-527-3887

Material Name: Diclofenac and Misoprostol Tablets

Trade Name:	ARTHROTEC
Synonyms:	Artotec, Misofenac, Arthotec
Chemical Family:	Mixture
Intended Use:	Pharmaceutical product used as non-steroidal, anti-inflammatory drug (nsaid)

2. HAZARDS IDENTIFICATION

Appearance: White tablet
Signal Word: WARNING

Statement of Hazard: Harmful if swallowed.
Suspected of damaging the unborn child.

Additional Hazard Information:

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.

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.

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

EU Hazard Symbols:

Xn

2. HAZARDS IDENTIFICATION

EU Risk Phrases:

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

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

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings 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	%
Diclofenac Sodium	15307-79-6	239-346-4	T; R25; Xi,R36/38; Repr. Cat.2, R61; R52/53	8-15
Misoprostol	59122-46-2	Not Listed	T;R25 Repr.Cat.1;R60-61	<1.0
Corn Starch	9005-25-8	232-679-6	Not Listed	*
Silicon dioxide, colloidal NF	7631-86-9	231-545-4 418-260-2	Not Listed	*
Talc (non-asbestiform)	14807-96-6	238-877-9	Not Listed	*
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Magnesium stearate	557-04-0	209-150-3	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Lactose Monohydrate	64044-51-5	Not Listed	Not Listed	*
Povidone	9003-39-8	Not Listed	Not Listed	*
Hydroxypropyl methylcelluslose	9004-65-3	Not Listed	Not Listed	*
Crospovidone	9003-39-8	Not Listed	Not Listed	*
Hydrogenated castor oil	8001-78-3	232-292-2	Not Listed	*
Triethyl Citrate	77-93-0	201-070-7	Not Listed	*
Methacrylic acid copolymer	25086-15-1	Not Listed	Not Listed	*

Additional Information: * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

4. 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.

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.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.

Fire Fighting Procedures: During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

Fire / Explosion Hazards: Not applicable

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

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.

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

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

General 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.

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

Misoprostol
Pfizer OEL TWA-8 Hr: 0.7 µg/m^3

Corn Starch
ACGIH Threshold Limit Value (TWA) 10 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Australia TWA	10 mg/m^3
Belgium OEL - TWA	10 mg/m^3
Bulgaria OEL - TWA	10.0 mg/m^3
Czech Republic OEL - TWA	4.0 mg/m^3
Greece OEL - TWA	10 mg/m^3 5 mg/m^3
Ireland OEL - TWAs	10 mg/m^3 4 mg/m^3
OSHA - Final PELS - TWAs:	15 mg/m^3
Portugal OEL - TWA	10 mg/m^3
Slovakia OEL - TWA	4 mg/m^3
Spain OEL - TWA	10 mg/m^3

Silicon dioxide, colloidal NF

Australia TWA	2 mg/m^3
Austria OEL - MAKs	4 mg/m^3
Czech Republic OEL - TWA	0.1 mg/m^3 4.0 mg/m^3
Estonia OEL - TWA	2 mg/m^3
Germany - TRGS 900 - TWAs	4 mg/m^3
Germany (DFG) - MAK	4 mg/m^3 inhalable fraction
Ireland OEL - TWAs	6 mg/m^3 2.4 mg/m^3
Latvia OEL - TWA	1 mg/m^3
OSHA - Final PELs - Table Z-3 Mineral D:	20 mppcf Listed
Slovakia OEL - TWA	4.0 mg/m^3
Slovenia OEL - TWA	4 mg/m^3

Talc (non-asbestiform)

ACGIH Threshold Limit Value (TWA)	2 mg/m^3
Australia TWA	2.5 mg/m^3
Austria OEL - MAKs	2 mg/m^3
Belgium OEL - TWA	2 mg/m^3
Bulgaria OEL - TWA	1.0 fiber/cm3 6.0 mg/m^3 3.0 mg/m^3
Czech Republic OEL - TWA	2.0 mg/m^3 10 mg/m^3
Denmark OEL - TWA	0.3 fiber/cm3
Finland OEL - TWA	0.5 fiber/cm3 5 mg/m^3
Greece OEL - TWA	10 mg/m^3 2 mg/m^3
Hungary OEL - TWA	2 mg/m^3
Ireland OEL - TWAs	10 mg/m^3 0.8 mg/m^3
Lithuania OEL - TWA	2 mg/m^3 1 mg/m^3
Netherlands OEL - TWA	0.25 mg/m^3
OSHA - Final PELs - Table Z-3 Mineral D:	20 mppcf
Poland OEL - TWA	4.0 mg/m^3 1.0 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Portugal OEL - TWA	2 mg/m^3
Romania OEL - TWA	2 mg/m^3
Slovakia OEL - TWA	2 mg/m^3 10 mg/m^3
Slovenia OEL - TWA	2 mg/m^3
Spain OEL - TWA	2 mg/m^3
Sweden OEL - TWAs	2 mg/m^3 1 mg/m^3

Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA)	10 mg/m^3
Australia TWA	10 mg/m^3
Belgium OEL - TWA	10 mg/m^3
Estonia OEL - TWA	10 mg/m^3
France OEL - TWA	10 mg/m^3
Ireland OEL - TWAs	10 mg/m^3 4 mg/m^3
Latvia OEL - TWA	2 mg/m^3
OSHA - Final PELS - TWAs:	15 mg/m^3
Portugal OEL - TWA	10 mg/m^3
Romania OEL - TWA	10 mg/m^3
Spain OEL - TWA	10 mg/m^3

Magnesium stearate

ACGIH Threshold Limit Value (TWA)	10 mg/m^3
Lithuania OEL - TWA	5 mg/m^3
Sweden OEL - TWAs	5 mg/m^3

Diclofenac Sodium

Pfizer Occupational Exposure Band (OEB): OEB2 (control exposure to the range of >100ug/m^3 to < 1000ug/m^3)

Analytical Method: Analytical method available for misoprostol. Contact Pfizer Inc for further information.

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.

Environmental Exposure Controls: Refer to specific Member State legislation for requirements under Community environmental legislation.

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
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

10. STABILITY AND REACTIVITY

Chemical Stability: Stable at normal conditions
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

11. TOXICOLOGICAL INFORMATION

General Information: The information included in this section describes the potential hazards of the individual ingredients.

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 methylcelluslose
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 > 1.43 mg/L
Mouse Oral LD 50 27 mg/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)

11. TOXICOLOGICAL INFORMATION

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

Diclofenac Sodium
Skin Irritation Positive
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) Negative

Diclofenac Sodium
Bacterial Mutagenicity (Ames) *Salmonella* Negative

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

11. TOXICOLOGICAL INFORMATION

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

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

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):

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) EC-50 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) EC-50 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.

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

EU Symbol: T
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.

EU Safety Phrases:
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
WARNING
Harmful if swallowed.
Suspected of damaging the unborn child.

Canada - WHMIS: Classifications

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

Diclofenac Sodium
Australia (AICS): Present

15. REGULATORY INFORMATION

EU EINECS/ELINCS List	239-346-4

Misoprostol

California Proposition 65	developmental toxicity initial date 4/1/90
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4

Lactose Monohydrate

Australia (AICS):	Present

Corn Starch

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	232-679-6

Povidone

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present

Hydroxypropyl methylcelluslose

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4

Crospovidone

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present

Silicon dioxide, colloidal NF

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	231-545-4 418-260-2

Hydrogenated castor oil

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	232-292-2

Talc (non-asbestiform)

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	238-877-9

Microcrystalline cellulose

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	232-674-9

Magnesium stearate

15. REGULATORY INFORMATION

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	209-150-3

Triethyl Citrate

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	201-070-7

Methacrylic acid copolymer

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

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: Pfizer proprietary drug development information.

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 4 - First Aid Measures. Updated Section 7 - Handling and Storage. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 15 - Regulatory Information.

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

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without 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