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

Product Identifier

Material Name: Dinoprostone Vaginal Tablets (Suppositories)

Trade Name: PROSTIN E2

Chemical Family: Mixture

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

Intended Use: Pharmaceutical product used for smooth muscle stimulation

Details of the Supplier of the Safety Data Sheet

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-800-879-3477

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

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

Contact E-Mail: pfizer-MSDS@pfizer.com

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Reproductive Toxicity: Category 1A

Label Elements

Signal Word: Danger

Hazard Statements: H360FD - May damage fertility. May damage the unborn child.

Precautionary Statements:
P201 - Obtain special instructions before use
P202 - Do not handle until all safety precautions have been read and understood
P280 - Wear protective gloves/protective clothing/eye protection/face protection
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations

PZ00257
3. COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>GHS Classification</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Dinoprostone</td>
<td>363-24-6</td>
<td>206-656-6</td>
<td>Acute tox. 4 (H302)</td>
<td>&lt;0.5</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Repr.1A (H360FD)</td>
<td></td>
</tr>
<tr>
<td>Corn Starch</td>
<td>9005-25-8</td>
<td>232-679-6</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>9004-34-6</td>
<td>232-674-9</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Silica colloidal, Ph. Eur.</td>
<td>112945-52-5</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
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<tr>
<td>Magnesium Stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>*</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose Monohydrate</td>
<td>64044-51-5</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

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 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: Wash skin with soap and water. If irritation occurs or persists, get 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 firefighting 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. Cleanup 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.

**Dinoprostone**

- Pfizer OEL TWA-8 Hr: 0.5 µg/m³, Skin

**Corn Starch**

- ACGIH Threshold Limit Value (TWA): 10 mg/m³
- Australia TWA: 10 mg/m³
- Belgium OEL - TWA: 10 mg/m³
- Bulgaria OEL - TWA: 10.0 mg/m³
### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**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). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

**Hands:**

Impervious disposable gloves (e.g. Nitrile, etc.) (double recommended) if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)

**Eyes:**

Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)

<table>
<thead>
<tr>
<th>Material Name: Dinoprostone Vaginal Tablets (Suppositories)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Czech Republic OEL - TWA</strong> 4.0 mg/m³</td>
</tr>
<tr>
<td><strong>Greece OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Ireland OEL - TWAs</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>OSHA - Final PELS - TWAs:</strong></td>
</tr>
<tr>
<td><strong>Portugal OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Slovakia OEL - TWA</strong> 4 mg/m³</td>
</tr>
<tr>
<td><strong>Spain OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Switzerland OEL -TWAs</strong> 3 mg/m³</td>
</tr>
<tr>
<td><strong>Silica colloidal, Ph. Eur.</strong></td>
</tr>
<tr>
<td><strong>ACGIH Threshold Limit Value (TWA)</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Austria TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Belgium OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Estonia OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>France OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Ireland OEL - TWAs</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Latvia OEL - TWA</strong> 2 mg/m³</td>
</tr>
<tr>
<td><strong>OSHA - Final PELS - TWAs:</strong></td>
</tr>
<tr>
<td><strong>Portugal OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Romania OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Russia OEL - TWA</strong> 6 mg/m³</td>
</tr>
<tr>
<td><strong>Spain OEL - TWA</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Switzerland OEL -TWAs</strong> 3 mg/m³</td>
</tr>
<tr>
<td><strong>Vietnam OEL - TWAs</strong> 10 mg/m³</td>
</tr>
<tr>
<td><strong>Silica colloidal, Ph. Eur.</strong></td>
</tr>
<tr>
<td><strong>Austria OEL - MAKs</strong> 4 mg/m³</td>
</tr>
<tr>
<td><strong>Germany (DFG) - MAK</strong> 4 mg/m³</td>
</tr>
<tr>
<td><strong>Switzerland OEL -TWAs</strong> 4 mg/m³</td>
</tr>
<tr>
<td><strong>Magnesium Stearate</strong></td>
</tr>
<tr>
<td><strong>Lithuania OEL - TWA</strong> 5 mg/m³</td>
</tr>
<tr>
<td><strong>Sweden OEL - TWAs</strong> 5 mg/m³</td>
</tr>
</tbody>
</table>

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**Revision date:** 12-Nov-2018

**Version:** 2.3

**Page:** 4 of 9

**Material Name:** Dinoprostone Vaginal Tablets (Suppositories)

**OSHA - Final PELS - TWAs:**

France OEL - TWA 10 mg/m³

OSHA - Final PELS - TWAs: 15 mg/m³
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Skin: Wear impervious protective clothing to prevent skin contact – consider use of disposable clothing where appropriate. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)

Respiratory protection: Under normal conditions of use, 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 (e.g. particulate respirator with a full mask, P3 filter). (Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.)

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State: Suppository
Odor: No data available.
Molecular Formula: Mixture
Color: White
Odor Threshold: No data available.
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)
Lactose Monohydrate
No data available
Corn Starch
No data available
Microcrystalline cellulose
No data available
Magnesium Stearate
No data available
Silica colloidal, Ph. Eur.
No data available
Dinoprost
Predicted 7.4 Log D 0.356
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

Flammability:
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 under normal conditions of use.
Possibility of Hazardous Reactions

PZ00257
10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Oxidizing Properties:</th>
<th>No data available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions to Avoid:</td>
<td>Fine particles (such as dust and mists) may fuel fires/explosions.</td>
</tr>
<tr>
<td>Incompatible Materials:</td>
<td>As a precautionary measure, keep away from strong oxidizers</td>
</tr>
<tr>
<td>Hazardous Decomposition Products:</td>
<td>No data available</td>
</tr>
</tbody>
</table>

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: Active ingredient may be harmful if swallowed. 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 fertility and the developing fetus.

Known Clinical Effects: Clinical use of this drug has caused hot flashes diarrhea nausea vomiting May cause low blood pressure and dizziness. Uterine contractions, vaginal bleeding, and prevention/termination of pregnancy have been seen in women taking this drug.

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

Lactose Monohydrate
Rat Oral LD50 29700 mg/kg

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

Dinoprostone
Rat Oral LD50 500 mg/kg
Rat Para-periosteal LD50 59.5mg/kg
Rat Subcutaneous LD50 31.6mg/kg
Mouse Oral LD50 750mg/kg
Mouse Intravenous LD50 23.2mg/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

Dinoprostone
Skin Sensitization - GPMT Guinea Pig Negative

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

Magnesium Stearate
13 Week(s) Rat Oral 1092 g/kg LOAEL Liver
11. TOXICOLOGICAL INFORMATION

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

**Dinoprostone**
- Embryo / Fetal Development: Mouse, Oral, 6 mg/kg, LOAEL, Fetotoxicity
- Embryo / Fetal Development: Rat, Oral, 6 mg/kg, LOAEL, Fetotoxicity
- Embryo / Fetal Development: Rat, Intraperitoneal, 12.5 mg/kg/day, LOEL, Teratogenic

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

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

**Dinoprostone**
- Bacterial Mutagenicity (Ames): *Salmonella*, Negative
- Direct DNA Damage: Negative
- Micronucleus: Negative

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

Silica colloidal, Ph. Eur.
- IARC: Group 3 (Not Classifiable)

12. ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been investigated. Releases to the environment should be avoided.

Toxicity: No data available

Persistence and Degradability: No data available

Bio-accumulative Potential: No data available

**Partition Coefficient: (Method, pH, Endpoint, Value)**

**Dinoprostone**
- Predicted: 7.4, Log D: 0.356

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

**Dinoprostone**
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
- EU EINECS/ELINCS List: 206-656-6

**Corn Starch**
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- 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

**Lactose Monohydrate**
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Australia (AICS): Present
- EU EINECS/ELINCS List: Not Listed

**Microcrystalline cellulose**
- 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: 232-674-9

**Silica colloidal, Ph. Eur.**
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Australia (AICS): Present
- EU EINECS/ELINCS List: Not Listed
15. REGULATORY INFORMATION

Magnesium Stearate

<table>
<thead>
<tr>
<th>Inventory - United States TSCA - Sect. 8(b)</th>
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</thead>
<tbody>
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<tr>
<td>CERCLA/SARA 313 Emission reporting</td>
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<tr>
<td>EU EINECS/ELINCS List</td>
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</tbody>
</table>

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Acute toxicity, oral-Cat.4; H302 - Harmful if swallowed
Reproductive toxicity-Cat.1A; H360FD - May damage fertility. May damage the unborn child.

Data Sources:
Pfizer proprietary drug development information. Publicly available toxicity information. Safety data sheets for individual ingredients.

Reasons for Revision:
Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 8 - Exposure Controls / Personal Protection.

Revision date:
12-Nov-2018

Prepared by:
Product Stewardship Hazard Communication

Pfizer Inc believes that the information contained in this 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