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  

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  

Material Name: Nafarelin Acetate Nasal Solution  
Trade Name: Synarel; Nasanyl; Synrelina; Synarela  
Chemical Family: Mixture  
Intended Use: Pharmaceutical product for the treatment of Central Precocious Puberty endometriosis

2. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS List</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nafarelin Acetate</td>
<td>86220-42-0</td>
<td>Not listed</td>
<td>2</td>
</tr>
<tr>
<td>Acetic acid USP - glacial</td>
<td>64-19-7</td>
<td>200-580-7</td>
<td>*</td>
</tr>
<tr>
<td>Hydrochloric Acid</td>
<td>7647-01-0</td>
<td>231-595-7</td>
<td>**</td>
</tr>
<tr>
<td>Benzalkonium Chloride</td>
<td>61789-71-7</td>
<td>263-080-8</td>
<td>*</td>
</tr>
<tr>
<td>Sodium hydroxide</td>
<td>1310-73-2</td>
<td>215-185-5</td>
<td>**</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS List</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorbitol solution</td>
<td>50-70-4</td>
<td>200-061-5</td>
<td>*</td>
</tr>
<tr>
<td>Water</td>
<td>7732-18-5</td>
<td>231-791-2</td>
<td>*</td>
</tr>
</tbody>
</table>

Additional Information:  
* Proprietary  
** to adjust pH  

Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

3. HAZARDS IDENTIFICATION

Appearance: Clear, colorless to slightly yellow solution  
Signal Word: WARNING

Statement of Hazard: May cause reproductive system effects  
May cause harm to the unborn child.  
Possible carcinogen  

Short Term: May cause eye and skin irritation, Not a skin sensitizer, Not acutely toxic (based on components).  

Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on liver, blood.
MATERIAL SAFETY DATA SHEET

Material Name: Nafarelin Acetate Nasal Solution
Revision date: 02-Jan-2007

Known Clinical Effects: Adverse effects most commonly reported in clinical use include headache, hot flashes, changes in libido, vaginal dryness, acne, emotional lability, myalgia, decreased breast size and irritation of the nasal mucosa. Hypersensitivity reactions may also occur in susceptible individuals.

EU Indication of danger: Toxic to reproduction, Category 2
Carcinogenic: Category 3

EU Hazard Symbols: R40 - Limited evidence of a carcinogenic effect
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

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.

4. FIRST AID MEASURES

Eye Contact: Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. If irritation occurs or persists, get medical attention.

Skin Contact: Remove contaminated clothing. Wash skin with soap and water. If irritation occurs or persists, get medical attention.

Ingestion: Call a physician immediately.

Inhalation: Remove to fresh air. Consult a physician.

5. FIRE FIGHTING MEASURES

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

Hazardous Combustion Products: May include oxides of nitrogen.

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 spill with absorbent material. 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:** Avoid open handling. Minimize generation of mists. Use local exhaust or perform work under hood/fume cupboard. Avoid inhalation and contact with skin, eyes, and clothing. When handling, use appropriate personal protective equipment (see Section 8).

**Storage Conditions:** Store at room temperature in properly labeled containers. Keep away from heat, sparks and flames. Protect from light.

**Storage Temperature:** 25°C (77°F)

### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Nafarelin Acetate**

Pfizer OEL TWA-8 Hr: 15 ng/m³

**Acetic acid USP - glacial**

OSHA - Final PELS - TWAs: = 10 ppm TWA
ACGIH Threshold Limit Value (TWA) = 10 ppm TWA
ACGIH Threshold Limit Value (STEL) = 15 ppm STEL
Australia STEL = 15 ppm STEL
Australia TWA = 10 ppm TWA
Australia TWA = 25 mg/m³ TWA

**Hydrochloric Acid**

ACGIH Ceiling Threshold Limit: = 2 ppm Ceiling
Australia PEAK = 5 ppm Peak
Australia PEAK = 7.5 mg/m³ Peak

**Sodium hydroxide**

OSHA - Final PELS - TWAs: 2 mg/m³
ACGIH Ceiling Threshold Limit: = 2 mg/m³ Ceiling
Australia PEAK = 2 mg/m³ Peak

The exposure limit(s) listed for solid components are only relevant if dust or mist may be generated.

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

**Engineering Controls:** Engineering controls should be used as the primary means to control exposures.

**Personal Protective Equipment:**

- **Hands:** Chemical protective gloves
- **Eyes:** Safety glasses or goggles
- **Skin:** Wear protective clothing with long sleeves to avoid skin contact. Wash hands and arms thoroughly after handling this product.
- **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:
10. STABILITY AND REACTIVITY

| Stability: | Stable under normal conditions of use. |
| Conditions to Avoid: | Exposure to light . |
| Incompatible Materials: | None known |

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)

**Nafarelin Acetate**
- Rat Oral LD50 >50 mg/kg
- Rat Subcutaneous LD50 0.5 µg/kg
- Rat Intraperitoneal LD50 0.5 µg/kg
- Mouse Oral LD50 >100 mg/kg
- Mouse Subcutaneous LD50 >0.5 mg/kg

**Sodium hydroxide**
- Mouse IP LD50 40 mg/kg

**Sorbitol solution**
- Rat Oral LD50 15,900 mg/kg
- Mouse Oral LD50 17,800 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)

**Nafarelin Acetate**
- Eye Irritation Rabbit No effect
- Skin Irritation Rabbit No effect
- Skin Sensitization Guinea Pig Negative

**Sodium hydroxide**
- Eye Irritation Rabbit Severe
- Skin Irritation Rabbit Severe

**Hydrochloric Acid**
- Skin Irritation Severe
- Eye Irritation Severe

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

**Nafarelin Acetate**
- 28 Day(s) Rat Subcutaneous 2 µg/kg/day LOAEL Reproductive system
- 6 Month(s) Rat Intramuscular 2 µg/kg/day LOAEL Reproductive system
- 6 Month(s) Monkey Intramuscular 2 µg/kg/day LOAEL Reproductive system
18 Month(s)  Dog  Subcutaneous  32 µg/kg/day  LOAEL  Female reproductive system
1 Year(s)  Rat  Intramuscular  10 µg/kg/day  LOAEL  Reproductive system, Liver, Blood

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

Nafarelin Acetate
Reproductive & Fertility  Rat  Intramuscular  0.04 µg/kg/day  LOAEL  Reproductive toxicity
Reproductive & Fertility  Rat  Intramuscular  0.1 µg/kg/day  LOAEL  Reproductive toxicity, Neonatal mortality
Reproductive & Fertility  Rabbit  Intramuscular  0.18 µg/kg/day  LOAEL  Fetotoxicity
Reproductive & Fertility  Rat  Intramuscular  0.4 µg/kg/day  LOAEL  Maternal Toxicity, Fetotoxicity
Reproductive & Fertility  Mouse  Intramuscular  600 µg/kg/day  NOAEL  Negative

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

Nafarelin Acetate
Bacterial Mutagenicity (Ames)  Salmonella , E. coli  Negative
Chromosome Aberration  Chinese Hamster Ovary (CHO) cells  Negative
Mitotic Gene Conversion  Fungi  Negative
In Vivo Micronucleus  Mouse  Negative

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

Nafarelin Acetate
18 Month(s)  Mouse  Intramuscular  500 µg/kg/day  LOAEL  Benign tumors
2 Year(s)  Rat  Intramuscular  10 µg/kg/day  LOAEL  Benign tumors

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

Hydrochloric Acid
IARC:  Group 3

12. ECOLOGICAL INFORMATION

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

13. DISPOSAL CONSIDERATIONS

Disposal Procedures:  Dispose of waste in accordance with all applicable laws and regulations.

14. TRANSPORT INFORMATION

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

EU Symbol: T
EU Indication of danger: Toxic to reproduction, Category 2
Carcinogenic: Category 3

EU Risk Phrases:
R40 - Limited evidence of a carcinogenic effect
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

EU Safety Phrases:
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
WARNING
May cause reproductive system effects
May cause harm to the unborn child.
Possible carcinogen

Canada - WHMIS: Classifications

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

Nafarelin Acetate
California Proposition 65
developmental toxicity, initial date 4/1/90

Acetic acid USP - glacial
CERCLA/SARA Hazardous Substances = 2270 kg final RQ
and their Reportable Quantities: = 5000 lb final RQ
Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
Standard for the Uniform Scheduling Schedule 2
for Drugs and Poisons:
Schedule 5
Schedule 6
EU EINECS List 200-580-7

Hydrochloric Acid
CERCLA/SARA 313 Emission reporting = 1.0 % de minimis concentration acid aerosols including mists,
vapor, gas, fog, and other airborne forms of any particle size

CERCLA/SARA Hazardous Substances = 2270 kg final RQ
and their Reportable Quantities: = 5000 lb final RQ
CERCLA/SARA - Section 302 Extremely Hazardous = 500 lb TPQ gas only
TPQs
CERCLA/SARA - Section 302 Extremely Hazardous = 5000 lb EPCRA RQ gas only
Substances EPCRA RQs
Inventory - United States TSCA - Sect. 8(b) T
Australia (AICS): Present
16. OTHER INFORMATION

Reasons for Revision: Updated Section 3 - Hazard Identification. Updated Section 6 - Accidental Release Measures.
Updated Section 8 - Exposure Controls / Personal Protection.

Prepared by: Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety

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.

End of Safety Data Sheet