

**SAFETY DATA SHEET 91/155/EEC**

**MS-275**

Version: 3.3 - 2007.01.02

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**1. Identification of the substance/preparation and the company**

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|-----|-----------------------------|--|
| 1.1 | Trade name:                 | MS-275   |
| 1.2 | Use:                        | pharmaceutical drug substance  |
| 1.3 | Company:                    | Bayer Schering Pharma AG<br>13342 Berlin, Germany<br>Telephone: +49-30-468-15343 |
| 1.4 | Emergency telephone number: | Schering fire brigade<br>Telephone: +49-30-468-14208                             |
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**2. Composition/information on ingredients**

**Chemical characterization**

3-Pyridylmethyl N-{4-[(2-aminophenyl)carbamoyl]benzyl}carbamate

ZK-No.: 244894

Formula: C<sub>21</sub> H<sub>20</sub> N<sub>4</sub> O<sub>3</sub>

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**3. Hazards identification**

- 3.1 Toxic if swallowed.  
Toxic: danger of serious damage to health by prolonged exposure if swallowed.  
May cause harm to the unborn child.  
Possible risk of impaired fertility.
- 3.2 May cause dust explosions in fine crystalline form.
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**4. First aid measures**

- |                 |  |
|-----------------|--|
| General advice: | Take off contaminated clothing and shoes immediately.<br>Call a physician immediately.   |
| Skin contact:   | In case of skin contact with powders or solution immediately rinse the areas affected continuously with water and then wash with soap and water.<br>Do NOT use solvents or thinners. |
| Eye contact:    | Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes.   |
| Ingestion:      | Rinse mouth.   |
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**5. Fire-fighting measures**

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|-----|---|--|
| 5.1 | Suitable extinguishing media:                   | carbon dioxide (CO <sub>2</sub> )<br>dry powder<br>foam<br>Water spray jet                 |
|     | Unsuitable extinguishing agents:                | high volume water jet  |
| 5.2 | Thermal decomposition:                          | nitrogen oxides (NO <sub>x</sub> )<br>carbon dioxide (CO <sub>2</sub> )<br>carbon monoxide |
| 5.3 | Special protective equipment for fire-fighters: | In the event of fire, wear self-contained breathing apparatus.                             |

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**6. Accidental release measures**

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|--------------------------|--|
| Methods for cleaning up: | Use mechanical handling equipment.<br>Avoid dust formation.<br>Pack separately and send back to manufacturer.<br>Flush with plenty of water.<br>Dispose of wastewater according to paragraph 13. |
| Additional advice:       | no data available  |

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**7. Handling and storage**

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|-----|--|---|
| 7.1 | Handling                                       |   |
|     | Hygiene measures:                              | Smoking, eating and drinking should be prohibited in the application area.<br>Use protective skin cream before handling the product.<br>Wash hands and face before breaks and immediately after handling the product. |
|     | Advice on safe handling:                       | Measures must be taken to prevent dust explosion when processing in fine crystalline form.<br>Avoid contact with skin, eyes and clothing.   |
| 7.2 | Storage  |   |
|     | Requirements for storage areas and containers: | Keep tightly closed in a dry, cool and well-ventilated place.<br>Protect from light.  |

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**8. Exposure controls / personal protection**

8.1 Exposure limit(s)

Control parameters	Basis
0,1 mg/m <sup>3</sup>	POEL (Preliminary Occupational Exposure Limit)

8.2 Personal protective equipment

Respiratory protection: respirator with P3 filter

Eye protection: safety glasses with side-shields

Hand protection: During the handling of the substance according to the intended use protection gloves from nitrile rubber have been proved. During the handling of pure solid substances or powder mixtures a permeation of the rubber material is not to be expected. In case of doubt, especially during handling of the substance together with organic solvents, the stability of the protection gloves has to be clarified with the manufacturer.

Skin and body protection: Choose body protection according to the amount and concentration of the dangerous substance at the work place.

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**9. Physical and chemical properties**

9.1 Form: powder

9.2 Colour: white

9.3 Odour: no data available

9.4 Change in physical state

Melting point/range : 156,0 - 160,0 °C

9.5 Density / Bulk density

no data available

9.6 Vapour pressure: < 1 mPa  
at 25 °C

9.7 Viscosity

no data available

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9.8 Solubility / Miscibility

Water solubility: 0,016 g/l  
at 20 °C

9.9 log Pow: 1,48

9.10 pH: no data available

9.11 Flash point: no data available

9.12 Ignition temperature: no data available

9.13 Explosion limits

no data available

9.14 Dust explosion class: 1 (3 µm)

9.15 Minimum ignition energy: no data available

9.16 Hygroscopicity: no data available

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**10. Stability and reactivity**

10.1 Conditions to avoid: no data available

10.2 Materials to avoid: no data available

10.3 Hazardous decomposition products

Thermal decomposition: nitrogen oxides (NO<sub>x</sub>)  
carbon dioxide (CO<sub>2</sub>)  
carbon monoxide

Hydrolytic decomposition: none reasonably foreseeable

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**11. Toxicological information**

Acute oral toxicity: LD50 mouse  
Dose: 380 - 750 mg/kg

Acute oral toxicity: NOEL rat  
Dose: < 1 mg/kg  
Remarks: 28-day

Acute oral toxicity: LD50 rat  
Dose: 150 - 200 mg/kg  
Method: OECD 423

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Toxic to reproduction (RE) : self classification 2

Toxic to reproduction (RF) : self classification 3

**Toxicological assessment**

**Mode of action:**

MS-275 is an inhibitor of histone deacetylase in tumor therapy.

**Acute toxicity:**

Accordingly, the uptake of major amounts of MS-275 may cause acute intoxication.

**Subacute toxicity:**

In studies with repeated oral administration of MS-275 over 28 days, effects in the haemopoietic tissue (bone marrow, spleen) occurred at doses of 1 mg/kg and 3 mg/kg in rats. The effects were partly reversible. In dogs, similar effects were observed at 0.3 mg/kg. These were fully reversible. In studies over 23 weeks in rats and monkeys, in which MS-275 was administered orally, signs of general intolerance were observed in the rat from 2.5 mg/kg/day, whereas changes in the haemopoietic tissue occurred from 0.1 mg/kg/day. The spermatogenesis was impaired from a dose of 0.5 mg/kg/day. In the monkey slight signs of intolerance were noted at a dose from 0.1 mg/kg/day onwards, whereas changes in the haemopoietic tissue occurred from 0.32 mg/kg/day.

**Mutagenic effect:**

Neither in vitro in the Ames-Test and the test with mouse lymphoma cells, nor in vivo in the mouse micronucleus test an indication for a mutagenic potential was found.

**Reproduction toxicology:**

In studies regarding embryotoxicity in rats and rabbits significant anomalies of the skeletal development as well as the survival rate of the fetuses (rats) and of the development of the vascular system were observed at doses which were not toxic in dams. Accordingly, MS-275 has to be labeled as embryotoxic and teratogenic.

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**12. Ecological information**

**Ecotoxicity effects**

Toxicity to fish:	LC50
	Species: danio rerio
	Dose: > 23,3 mg/l
	Exposure time: 96 h
	Method: OECD Test Guideline 203, Paris, 1981
	Remarks:
	saturated aqueous solution

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Toxicity to daphnia:	EC50 Species: Daphnia Dose: > 18,8 mg/l Exposure time: 48 h Method: OECD Test Guideline 202, Paris, 1981 Remarks: saturated aqueous solution
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Toxicity to algae:	EC50 Species: Chlorella vulgaris Dose: > 16,6 mg/l Exposure time: 72 h Method: OECD Test Guideline 201, Paris, 1981 Remarks: saturated aqueous solution
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**Biodegradability**

Aquatic:	Not readily biodegradable.  not toxic to the microbes of activated sludge
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**13. Disposal considerations**

Product:	Dissolve or suspend cautiously in a flammable solvent and incinerate in a combustion plant for chemical waste.
Waste code:	07 05 08

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**14. Transport information**

14.1 Land transport - ADR

Class:	6.1
Risk No.:	60
UN-No:	2811
ADR/RID-Labels:	6.1
Packaging group:	III
Description of the goods:	TOXIC SOLID, ORGANIC, N.O.S. (3-PYRIDYLMETHYL N-{4-[(2-AMINOPHENYL)CARBAMOYL]BENZYL}CARBAMATE)

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**14.2 Sea transport - IMDG**

IMDG-Code:	6.1
EmS:	6.1-04
UN-No:	2811
Packaging group:	III
Marine pollutant:	no data available
Description of the goods:	TOXIC SOLID, ORGANIC, N.O.S. (3-PYRIDYLMETHYL N-{4-[(2-AMINOPHENYL)CARBAMOYL]BENZYL}CARBAMATE)

**14.3 Air transport - ICAO/IATA**

IATA-DGR:	6.1
UN/ID No.:	2811
Packaging group:	III
Description of the goods:	TOXIC SOLID, ORGANIC, N.O.S. (3-PYRIDYLMETHYL N-{4-[(2-AMINOPHENYL)CARBAMOYL]BENZYL}CARBAMATE)

**15. Regulatory information**

**15.1 Labelling according to EEC Directive**

Symbol(s):	T	Toxic
R-phrases(s):	R25 R48/25  R61 R62	Toxic if swallowed. Toxic: danger of serious damage to health by prolonged exposure if swallowed. May cause harm to the unborn child. Possible risk of impaired fertility.
S-phrases(s):	S22 S36/37 S45	Do not breathe dust. Wear suitable protective clothing and gloves. In case of accident or if you feel unwell, seek medical advice immediately (show label where possible).

**15.2 National legislation**

Germany

Water contaminating class (Germany):	3 Appendix 3 VWWWS 07/05
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German storage class:	6.1A - Combustible substances, toxic
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Pharmaceutical substance  
class:

G3  
Estimation from toxicological studies (pSOEL)

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**16. Other information**

**Further information**

Changes made since the last version are highlighted in the margin. This version replaces all previous versions.

The above information is based on our present knowledge and experience and is intended as a description of the safety requirements for our product. It is not intended as an assurance that the product in question has certain properties.

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