



# MATERIAL SAFETY DATA SHEET

Revision date: 21-Jul-2011

Version: 1.0

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

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### Material Name: Tilidine Hydrochloride Drops

Trade Name:	VALORON
Synonyms:	Tilidine HCl Solution
Chemical Family:	Opiod
Intended Use:	Pharmaceutical product used as opioid analgesic

## 2. HAZARDS IDENTIFICATION

Appearance: Clear, colorless, liquid  
Signal Word: WARNING

Statement of Hazard: Harmful if swallowed.

### Additional Hazard Information:

**Short Term:** May cause central nervous system effects. May cause drowsiness, insomnia, nervousness, and dizziness. May cause eye irritation (based on components) .  
**Long Term:** Repeat-dose studies in animals have shown a potential to cause adverse effects on liver. This product contains ethanol which can cause liver changes, central nervous system effects, and birth defects in the developing fetus.

**Known Clinical Effects:** May cause effects similar to those seen in clinical use including fatigue, feelings of relaxation, unpleasantness or drunkenness, lightheadedness, nervousness, dizziness, nausea, vomiting, dry mouth, dry eyes, itching, and slow breathing and/or heart rate.

**EU Indication of danger:** Harmful

### EU Hazard Symbols:

Xn



### EU Risk Phrases:

R22 - Harmful if swallowed.  
Hazardous Substance. Dangerous Goods.

**Australian Hazard Classification (NOHSC):**

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### 2. HAZARDS IDENTIFICATION

**Note:** This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the product or its ingredients 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	%
Tilidine hydrochloride	27107-79-5	248-226-0	T;R25	10
Ethanol	64-17-5	200-578-6	F;R11	19

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Sodium propylparaben	35285-69-9	252-488-1	Not Listed	*
Sodium Methyl p-Hydroxybenzoate (methylparaben sodium)	5026-62-0	225-714-1	Not Listed	*
Sorbitol solution	50-70-4	200-061-5	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:** Fine particles (such as dust and mists) may fuel fires/explosions.

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### 6. ACCIDENTAL RELEASE MEASURES

<b>Health and Safety Precautions:</b>	Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.
<b>Measures for Cleaning / Collecting:</b>	Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.
<b>Measures for Environmental Protections:</b>	Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.
<b>Additional Consideration for Large Spills:</b>	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

<b>General Handling:</b>	Avoid breathing vapor or mist. 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.
<b>Storage Conditions:</b>	Store as directed by product packaging.

### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

<b>Tilidine hydrochloride</b>	
Pfizer OEL TWA-8 Hr:	50µg/m <sup>3</sup>
<b>Ethanol</b>	
ACGIH Threshold Limit Value (STEL)	1000 ppm
Australia TWA	1000 ppm
	1880 mg/m <sup>3</sup>
Austria OEL - MAKs	1000 ppm
	1900 mg/m <sup>3</sup>
Belgium OEL - TWA	1000 ppm
	1907 mg/m <sup>3</sup>
Bulgaria OEL - TWA	1000.0 mg/m <sup>3</sup>
Czech Republic OEL - TWA	1000 mg/m <sup>3</sup>
Denmark OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
Estonia OEL - TWA	500 ppm
	1000 mg/m <sup>3</sup>
Finland OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
France OEL - TWA	1000 ppm
	1900 mg/m <sup>3</sup>
Germany - TRGS 900 - TWAs	500 ppm
	960 mg/m <sup>3</sup>
Germany (DFG) - MAK	500 ppm
	960 mg/m <sup>3</sup>

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### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Greece OEL - TWA	1000 ppm 1900 mg/m <sup>3</sup>
Hungary OEL - TWA	1900 mg/m <sup>3</sup>
Ireland OEL - TWAs	1000 ppm 1900 mg/m <sup>3</sup>
Latvia OEL - TWA	1000 mg/m <sup>3</sup>
Lithuania OEL - TWA	500 ppm 1000 mg/m <sup>3</sup>
Netherlands OEL - TWA	260 mg/m <sup>3</sup>
OSHA - Final PELs - TWAs:	1000 ppm 1900 mg/m <sup>3</sup>
Poland OEL - TWA	1900 mg/m <sup>3</sup>
Portugal OEL - TWA	1000 ppm
Romania OEL - TWA	1000 ppm 1900 mg/m <sup>3</sup>
Slovakia OEL - TWA	500 ppm 960 mg/m <sup>3</sup>
Slovenia OEL - TWA	1000 ppm 1900 mg/m <sup>3</sup>
Spain OEL - TWA	1000 ppm 1910 mg/m <sup>3</sup>
Sweden OEL - TWAs	500 ppm 1000 mg/m <sup>3</sup>

<b>Engineering Controls:</b>	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.
<b>Environmental Exposure Controls:</b>	Refer to specific Member State legislation for requirements under Community environmental legislation.
<b>Personal Protective Equipment:</b>	Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).
<b>Hands:</b>	Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.
<b>Eyes:</b>	Wear safety glasses or goggles if eye contact is possible.
<b>Skin:</b>	Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.
<b>Respiratory protection:</b>	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

<b>Physical State:</b>	Liquid	<b>Color:</b>	Clear, colorless
<b>Odor:</b>	Alcohol, Menthol	<b>Molecular Formula:</b>	Mixture
<b>Molecular Weight:</b>	Mixture		
<b>pH:</b>	1.5 - 2.0		
<b>Specific Gravity:</b>	1.08 to 1.1(25 °C)		
<b>Polymerization:</b>	Will not occur		

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### 10. STABILITY AND REACTIVITY

**Chemical Stability:** Stable under normal conditions of use.  
**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)

##### **Tilidine hydrochloride**

Rat Oral LD50 < 200 (free base) mg/kg  
Rat Intragastric LD50 417.7 mg/kg  
Rat Intravenous LD50 71 mg/kg  
Rat Intramuscular LD50 387 mg/kg  
Rat Subcutaneous LD50 400 mg/kg

##### **Ethanol**

Mouse Oral LD50 3,450 g/m<sup>3</sup>  
Rat Oral LD50 7,060 mg/kg  
Mouse Inhalation LC50 4h 39 g/m<sup>3</sup>  
Rat Inhalation LC50 10h 20,000 ppm

##### **Sorbitol solution**

Rat Oral LD50 15,900 mg/kg  
Mouse Oral LD50 17,800 mg/kg

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

##### **Tilidine hydrochloride**

Skin Sensitization - GPMT Guinea Pig Negative

##### **Ethanol**

Eye Irritation Rabbit Severe

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

##### **Tilidine hydrochloride**

6 Month(s) Rat Oral 25 mg/kg/day NOAEL Liver  
6 Month(s) Dog Oral 25 mg/kg/day NOAEL None identified  
8 Month(s) Rat Subcutaneous 50 mg/kg/day LOEL Liver  
8 Month(s) Dog Intravenous 9 mg/kg/day NOAEL None identified

#### Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

##### **Tilidine hydrochloride**

Reproductive & Fertility Rat No route specified 50 mg/kg/day NOAEL No effects at maximum dose  
Embryo / Fetal Development Rat Oral 100 mg/kg/day NOAEL No effects at maximum dose  
Embryo / Fetal Development Rat Subcutaneous 25 mg/kg/day NOAEL No effects at maximum dose  
Embryo / Fetal Development Rabbit Oral 50 mg/kg/day NOAEL No effects at maximum dose  
Peri-/Postnatal Development Rat Oral 25 mg/kg/day NOAEL Neonatal toxicity

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## 11. TOXICOLOGICAL INFORMATION

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

#### Tilidine hydrochloride

Not specified Mouse No route specified 100 mg/kg/day NOEL Not carcinogenic

Not specified Rat No route specified 100 mg/kg/day NOEL Not carcinogenic

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

#### Ethanol

**IARC:** Group 1 (Carcinogenic to Humans)

**OSHA:** Listed

## 12. ECOLOGICAL INFORMATION

**Environmental Overview:** The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided.

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

#### Ethanol

Fingerling Trout NPDES LC50 24 Hours 11,200 mg/L

*Oncorhynchus mykiss* (Rainbow Trout) NPDES LC50 96 Hours 12,900 mg/L

*Pimephales promelas* (Fathead Minnow) NPDES LC50 96 Hours 14,200 mg/L

## 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:** Xn  
**EU Indication of danger:** Harmful

**EU Risk Phrases:** R22 - Harmful if swallowed.

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### 15. REGULATORY INFORMATION

#### EU Safety Phrases:

S23 - Do not breathe fumes/vapour/spray.  
S45 - In case of accident or if you feel unwell seek medical advice immediately (show the label where possible).

#### OSHA Label:

WARNING  
Harmful if swallowed.

#### Canada - WHMIS: Classifications

##### WHMIS hazard class:

Class D, Division 1, Subdivision B



#### Tilidine hydrochloride

U.S. Drug Enforcement Administration:	Schedule I
EU EINECS/ELINCS List	248-226-0

#### Ethanol

California Proposition 65	developmental toxicity initial date 10/1/87
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	200-578-6

#### Sodium propylparaben

Australia (AICS):	Present
EU EINECS/ELINCS List	252-488-1

#### Sodium Methyl p-Hydroxybenzoate (methylparaben sodium)

Australia (AICS):	Present
EU EINECS/ELINCS List	225-714-1

#### Sorbitol solution

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	200-061-5

### 16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

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R25 - Toxic if swallowed.

R11 - Highly flammable.

**Data Sources:**

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

**Prepared by:**

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

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**End of Safety Data Sheet**