



Aplidin 2 mg

MATERIAL SAFETY DATA SHEET

Edition : 19 Date : 28/10/2019

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## 1. CHEMICAL PRODUCT AND COMPANY INFORMATION

**Aplidin 2 mg**

**Relevant identified uses of The Substance or Mixture :**  
Finished Pharmaceutical Product.

### Company Information

Pharma Mar S.A.  
Avda. de los Reyes, 1  
28770 Colmenar Viejo - Madrid - ESPAÑA  
Phone (34) 91-846-6000

### Emergency :

Instituto Nacional de Toxicologia (24h) Phone : (34) 915-620-420  
Pharma Mar [09:00 - 17:00] Phone (34) 91-846 60 00

## 2. HAZARDS IDENTIFICATION

Hazard Category : ---

Signal Word ---

*Antitumor Active Pharmaceutical Ingredient.*

*For PLITIDEPSIN Drug Substance: Possible risks of irreversible effects. Harmful by inhalation, if swallowed and in contact with the skin.*

## 3. COMPOSITION / INFORMATION ON INGREDIENTS

Molecular Formula: ----

CAS Number : ----- *Plitidepsin*  
137219-37-5

Ingredient	CAS	%	Classification
PLITIDEPSIN	137219-37-5	1.96 %	Acute Toxicity : 1
D-Mannitol	69-65-8	98.04%	Not classified as hazardous

*Active Ingredient Drug Substance: PLITIDEPSIN: Didemnin A, N-[1-(1,2-dioxopropyl)-L-propyl]- (9CI) (2S)-N-[(1R)-1-[(3S,6R,7S,10R,11S,15S,17S,20S,25aS)-11-hydroxy-20-isobutyl-15-isopropyl-3-(4-methoxybenzyl)-2,6,17-trimethyl-10-[(1S)-1-methylpropyl]-1,4,8,13,16,18,21-heptaoxodocosahydro-15H-pyrrolo[2,1-f][1,15,4,7,10,20]dioxo tetraazacyclotricosin-7-yl]amino)-carbonyl]-3-methylbutyl]-N-methyl-1-pyrrovoylpyrrolidine-2-carboxamide*

## 4. FIRST AID MEASURES

Inhalation : *Remove to exposure to fresh air immediately. If not breathing, give artificial respiration. If breathing is difficult give oxygen*

Ingestion : *Wash mouth out with water. Only induce vomiting at instructions of a physician.*

Eye : *Flush eyes with plenty of water for at least 15 minutes.*

Skin : *Wash affected areas with plenty of soap and water for at least 15 minutes while removing contaminated clothing and shoes.*

## 5. FIRE FIGHTING MEASURES

Extinguishing media :	<i>Use Water, Dry Chemical, Carbon Dioxide or chemical Foam</i>
Unusual Hazard Special Risk:	<i>May include carbon monoxide, carbon dioxide &amp; oxides of nitrogen.</i>
Protective equipment:	<i>Wear self-contained breathing apparatus and protective clothing</i>





## 6. ACCIDENTAL RELEASE MEASURES

Personal Precautions :	<i>Wear protective equipment to avoid inhalation and skin/eye contact. Keep unprotected persons away.</i>
Environmental precautions :	<i>Take precautions to ensure product does not contaminate the ground or enter the drainage system</i>
Methods for spill and cleaning:	<i>Wipe up with absorbent towels/other absorbent material and place all material into a suitable container for disposal. Decontaminate.</i>

## 7. HANDLING AND STORAGE

Handling Precautions :	<i>Chemicals should be used only by those trained in handling potentially hazardous materials</i>
	<i>See relevant guidance for handling cytotoxic materials. Wear protective equipment to avoid inhalation and skin/eye contact.</i>
Storage :	<i>Store in tightly sealed containers. Protect from moisture. Drug is routinely stored between + 2 °C and + 8 °C</i>

## 8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

Engineering measures :	<i>Use laminar flow biological cabinet or adequate ventilation to keep airborne concentrations low.</i>
Hygiene practices:	<i>Remove/laundry contaminated clothing before re-use or dispose after single use. Wash thoroughly after handling.</i>
 Respiratory protection:	<i>Wear respirator fitted with particulate filter P2</i>
 Hands protection:	<i>Use appropriate gloves.</i>
 Eyes protection:	<i>Wear appropriate protective eyeglasses or chemical safety goggles.</i>
 Clothing:	<i>Wear appropriate protective clothing to prevent skin exposure.</i>



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## 9. PHYSICAL AND CHEMICAL PROPERTIES

Form:

*Powder*

Molecular Mass

*1110,34 For Plitidepsin DS*

Temperatures:

Boiling point :

*Not determined*

Odour:

*Not determined*

pH value:

*Not determined*

Melting point :

*186 °C*

Colour:

*White to off-white*

Vapour pressure:

*Not determined*

Flash point :

*Not determined*

Auto ignition point :

*Not determined*

Solubility in water : *Insoluble*

Solubility : *Freely soluble in Acetonitrile, Dichloromethane, Methanol, Ethanol, Ethyl Acetate and Isopropanol.*

## 10. STABILITY AND REACTIVITY

Conditions to be avoided : *Keep at a Temperature not exceeding + 8°C*

Substances to be avoided : *Not available.*

Hazardous decomposition : *Carbon monoxide, carbon dioxide & oxides of nitrogen.*

## 11. TOXICOLOGICAL INFORMATION

LD50 Oral rats:

Not Determined

*For Plitidepsin Drug Substance: MTD rat: 570 µg/Kg (Intravenous toxicity in Wistar Rat Single-dose)*

*Drug Substance, In Vitro Activity IC50(M): BLADDER 5637 IC50m: 2.2·10E-8 BREAST BT-20 IC50mean: 1.7·10E-7 GASTIC Hs746T IC50m: 2.0·10E-7 MELANOMA SK-MEL-28 IC50m: 6.5·10E-7 NEUROBLASTOMA SK-N-MC IC50m: 1.2·10E-8 LEUKEMIA HL-60 IC50m: 1.1·10E-8*

*Drug Substance: Mutagenic Standard Ames test : Negative*

## 12. ECOLOGICAL INFORMATION.

Environmental effects :

*Not determined*

## 13. DISPOSAL CONSIDERATIONS.

Official Regulations : *State and local disposal regulations may differ from federal disposal regulations. Dispose of container and unused contents in accordance with federal, state and local*

Waste Disposal Methods : *Whatever cannot be saved for recovery or recycling should be managed in an appropriate and approved waste disposal facility. Processing, use or contamination of this product may change the waste management options.*



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#### 14. TRANSPORT INFORMATION

UN Number : Information : Transport symbol

--- Not regulated as a dangerous goods

##### ADR / RID

##### IATA

##### IMDG

Class: --- Class: --- Instruc --- Class: ---

Danger: --- PG (Oral) : --- PG: ---

PG: --- Inhalation PG I : No MFAG: ---

This material is NOT classed as having an 'Inhalation Hazard' as defined by IATA and ICAO Regulations.

#### 15. REGULATORY INFORMATION

Labelling according to EC Directives :

Signal Word : --- SYMBOLS

Hazard Category : ---

##### Hazard and precautionary statements

Not a hazardous substance or mixture according to Regulation (EC) No. 1272/2008.

According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008.

Medicinal products in the finished state for human use as defined in 2001/83/EC, are exempted from classification and other criteria of 1272/2008.

##### 15.2 Chemical safety assessment

A Chemical Safety Assessment is not applicable (mixture)

#### 16. OTHER INFORMATION.

Revision : **19** Investigator Brochure APLIDIN (plitidepsin) Version 19.0 May 2019

EC Directive Current. The information above is believed to be accurate and represents the best information currently available to us. However, we make no warranty of merchantability or any other warranty, express or implied, with respect to such information, and we assume no liability resulting from its use. Users should make their own investigations to determine the suitability of the information for their particular purposes. In no way shall the company be liable for any claims, losses or damages of any third party or for lost profits or any special, indirect, incidental, consequential or exemplary damages, howsoever arising, even if the company has been advised of the possibility of such damages.

##### Abbreviations and acronyms

ADR: European Agreement concerning the International Carriage of Dangerous Goods by Road - CAS: Chemical Abstracts Service (division of the American Chemical Society) - ICAO: International Civil Aviation Organisation

IMDG: International Maritime Code for Dangerous Goods - IATA: International Air Transport Association - GHS: Globally Harmonised System of Classification and Labelling of Chemicals - RID: Regulations Concerning the International Transport of Dangerous Goods by Rail)