

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Aplidin 2 mg

Pharma Mar S.A. Sociedad Unipersonal
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 : **Acute Toxicity : 4**

Signal Word **Warning**

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

6. ACCIDENTAL RELEASE MEASURES

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

7. HANDLING AND STORAGE

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

8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

- Engineering measures : *Use laminar flow biological cabinet or adequate ventilation to keep airborne concentrations low.*
- Hygiene practices: *Remove/laundry contaminated clothing before re-use or dispose after single use. Wash thoroughly after handling.*



Respiratory protection: *Wear respirator fitted with particulate filter P2*



Hands protection: *Use appropriate gloves.*



Eyes protection: *Wear appropriate protective eyeglasses or chemical safety goggles.*



Clothing: *Wear appropriate protective clothing to prevent skin exposure.*

9. PHYSICAL AND CHEMICAL PROPERTIES

<u>Form:</u>	<u>Molecular Mass</u>	<u>Temperatures:</u>	
Powder	1110,34 For Plitidepsin DS	Boiling point :	Not determined
<u>Odour:</u>	<u>pH value:</u>	Melting point :	186 °C
Not determined	Not determined	Flash point :	Not determined
<u>Colour:</u>	<u>Vapour pressure:</u>	Auto ignition point :	Not determined
White to off-white	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)

Health effects :

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.

14. TRANSPORT INFORMATION

UN Number : Information :
3249 MEDICINE, SOLID, TOXIC, N.O.S

Transport symbol



ADR / RID	IATA	IMDG
Class: 6.1	Class: 6.1 Instruc ---	Class: ---
Danger: 60	PG (Oral) : III	PG: ---
PG: III	Inhalation PG I : No	MFAG: ---

Active Pharmaceutical Ingredient is neither explosive, nor oxidizing, poisonous/toxic, infectious, radioactive, corrosive or magnetic, and its close cup flash point is over 67.5°C (141°F) according to IATA and ICAO

15. REGULATORY INFORMATION

Labelling according to EC Directives :

Signal Word : **Warning**

SYMBOLS

Hazard Category : **Acute Toxicity : 4**



GHS07

Hazard and precautionary statements

- H302 Harmful if swallowed.
- P264 Wash thoroughly after handling.
- P270 Do not eat, drink or smoke when using this product.
- P301+ P312 IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell.
- P330 Rinse mouth.
- P405 Store locked up.
- P501 Dispose of contents/containers in accordance with local regulation

16. OTHER INFORMATION.

Revision Number **14** Date **06/08/2014**

Reference : [14] IB Aplidin Edition 14.0 May 2014

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.