

## Safety Data Sheet (2001/58/EU)

Perifosin (D-21266)

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<b>1.</b>	<b>Name of Substance/Preparation and Firm</b>
<b>Substance</b>	Perifosin (D-21266)
<b>Use</b>	Drug, Cytostatic
<b>Manufacturer/Supplier</b>	Zentaris GmbH Daimlerstr. 40 D-60314 Frankfurt a.M.
<b>Tel.</b>	069-42602-0
<b>Fax.</b>	069-42602-3413
<b>Emergency Information</b>	06131-19240 (24 h) - Mainz University Hospital Centre for Information on Poisons

<b>2.</b>	<b>Composition/Information on Components</b>	
<b>Chemical Characterisation (single substance)</b>	<i>Name of the Substance</i> D-21266 Perifosin (D-21266) 4-[[Hydroxy(octadecyloxy)phosphinyl]oxy]-1,1-dimethylpiperidine, internal salt	
	<i>Chemical Formula</i> C <sub>25</sub> H <sub>52</sub> NO <sub>4</sub> P	
	<i>CAS No.</i> 157716-52-4	
	<i>EINECS No./ELINCS No.</i> No information	
	<i>Code Letter</i>	<i>R Code</i>
	T	R 60-61-64-22-48/25
<b>Additional Comment</b>	Caution: This substance has not yet been fully investigated.	

<b>3.</b>	<b>Possible Risks</b>
<b>Type of Risk</b>	Repr. Cat. 2 (R <sub>F</sub> 2, R <sub>E</sub> 2) T poisonous Xn Harmful to health
<b>Specific Human or Environmental Risks</b>	Can impair reproduction. Can harm the foetus in the womb. Can harm babies through the mother's milk. Harms health when swallowed. Poisonous: Danger of severe harm to health after long exposure by swallowing

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<b>4.</b>	<b>First-Aid Measures</b>
<b>General Comments</b>	Take the affected person out of the danger area. Do not leave the affected person without supervision. Take off contaminated or soaked clothing immediately and remove it safely.
<b>After Inhalation</b>	Take affected person into fresh air and let him lie in peace. See for medical care.
<b>After Skin Contact</b>	After skin contact, rinse immediately with a lot of water. If there is continued skin irritation, visit a doctor.
<b>After Eye Contact</b>	Open the eye-slit and rinse immediately and thoroughly with a lot of water for at least 5 min. Subsequent treatment from an ophthalmologist.
<b>After Swallowing</b>	Cause the patient to vomit. This must be independently and in a state of full consciousness. Rinse the mouth with water and get the patient to drink a lot of water. Seek medical assistance.
<b>Comments for the Doctor</b>	See too section 3. Drug, cytostatic After swallowing: Damage possible to kidneys, eyes, skin, gastrointestinal tract, reproductive organs (testicles, ovaries). Symptoms: Gastrointestinal symptoms - nausea, vomiting Specific recommendations: control of renal function and electrolyte balance.

<b>5.</b>	<b>Measures for Fighting Fires</b>
<b>Suitable Extinguishing Agent</b>	All extinguishing agents are suitable. Agree on how to put out the fire at its site.
<b>Unsuitable Extinguishing Agent</b>	Not known
<b>Special Risks from the Substance, its Combustion Products or the Resulting Gases</b>	See section 3. Toxic pyrolysis products and nitrogen oxides may be released on combustion.
<b>Special Protective Equipment</b>	In case of fire, wear respiratory protective equipment which is independent of the surroundings and a chemical safety suit.
<b>Additional Comments</b>	Fire residues and contaminated fire water must be disposed of in accordance with local official regulations. Fire water may not get into the drains or water.

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<b>6.</b>	<b>Measures after Accidental Release</b>
<b>Individual Precautions</b>	Wear personal protective clothing; See section 8.
<b>Precautions to Protect the Environment</b>	Do not let it get into the soil or water.
<b>Procedure for Cleaning or Uptake</b>	Take up moist and collect in a suitable container. Avoid dust formation. Clean contaminated areas thoroughly with water.
<b>Additional Comments</b>	Dispose of contaminated material as waste, as in Section 13.

<b>7.</b>	<b>Handling and Storage</b>
<b>Handling</b>	<i>Comments on Safe Handling</i> The product should only be handled by trained personnel in defined working areas. See that there is suitable suction or ventilation at the place of work (safety workbench) or for the machines used. Always close containers well after product has been taken.
	<i>Comments on Prevention of Fire and Explosion</i> Avoid effects of heat and sources of ignition. Avoid dust formation. Take measures against electrostatic charging. Further information: See that there are suitable possibilities for retaining fire water. See fire water retention guideline (LÖRÜRL).
<b>Storage</b>	<i>Requirements for Storage Rooms and Containers</i> The substance is hygroscopic! Only store tightly closed in the original container and in a dry cool and well ventilated place under 25°C. Avoid air moisture.
	<i>Comments on Storage with Other Materials</i> No information
	<i>Further Comments on Storage Conditions</i> Keep under lock, with access only to trained persons.
	<i>Storage Class</i> LKG 6.1 B

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<b>8.</b>	<b>Limits to Exposure and Personal Protective Equipment</b>
<b>Additional Comments on the Planning of Technical Plants</b>	See Section 7; No further comments are necessary.
<b>Components with limits for the place of work which must be monitored</b>	<i>Name of the Substance</i> D-21266 Perifosin (D-21266) 4-[[Hydroxy(octadecyloxy)phosphinyl]oxy]-1,1-dimethylpiperidine, internal salt
	<i>CAS No</i> 157716-52-4
	<i>Limits / Value / Unit</i> No data available
<b>Additional Comments</b>	See section 3. When processing the product, the air at the place of work must be regularly controlled and the exposed employee must be regularly monitored.
<b>Personal Protective Equipment</b>	The personal protective equipment must correspond to the requirements of guideline 89/686/EEC with amendments (CE mark). This must be laid down for the place of work in the context of a risk assessment, in accordance with guideline 89/686/EEC with amendments.
	<i>General Protective and Hygienic Measures</i> The usual protective measures when working with chemicals must be observed. Do not eat, drink, smoke or take snuff at work. Wash hands before breaks and at the end of work. If contact with skin or eyes is possible, use the recommended hand/eye/body protection. Store clothing separately. Working clothes should not be worn outside the area of work. Change wetted or soaked clothing.
	<i>Respiratory Protection</i> If open work is unavoidable: Wear respiratory protection equipment with particle filter P3.
	<i>Hand protection</i> Rubber Gloves
	<i>Eye Protection</i> If open work is unavoidable: Wear safety glasses with lateral protection.
	<i>Body Protection</i> Wear protective clothing. Avoid contamination of clothing with product.

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<b>9.</b>	<b>Physical and Chemical Properties</b>
<b>Form</b>	Solid, powder
<b>Colour</b>	White
<b>Odour</b>	Odourless

	Value / Range / Unit
Change of state	
Melting Point / Range	270-271 °C
Method	
Boiling point / Boiling range	n.d.
Method	
Flash Point	n.d.
Method	
Ignitability	n.d.
Method	
Ignition Temperature	n.d.
Method	
Spontaneous Ignitability	n.d.
Method	
Explosion Limits	
Dust Explosion	n.d.
Lower	
Upper	
Method	
Max. Abs, Explosion Pressure	
Dust explosion class	
Vapour Pressure	n.d.
Method	
Density	n.a.
Method	
Bulk Density	n.d.
Method	
Solubility	ca. 300 g/l
Medium	
Water (at 25°C)	
Method	
pH	5.8
Medium	
(0.2 g/l water) (at 20°C)	
Distribution Coefficient	Log pOW>4.6
n-Octanol/Water Comp.:	
pH 7-12	
Viscosity	n.a.
Method	
Additional Comments	none

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<b>10.</b>	<b>Stability and reactivity</b>
<b>Conditions to be Avoided</b>	Hygroscopic Avoid air moisture With expert handling and storage, no dangerous reactions are known.
<b>Substances to be Avoided</b>	None known
<b>Dangerous Decomposition Products</b>	None known
<b>Additional Comments</b>	None

<b>11.</b>	<b>Information on Toxicology</b>
<b>Acute Toxicity</b>	<i>LD/LC values relevant to rating</i> Acute oral toxicity: LD <sub>50</sub> =649 mg/kg, rat (male and female), OECD 401 Acute oral toxicity: LD <sub>50</sub> =975 mg/kg, mouse (male and female), OECD 401
<b>Primary Irritation</b>	n.d.
<b>Sensitisation</b>	n.d.
<b>Effects after repeated or protracted exposure (subacute to chronic toxicity)</b>	Rat oral, 13 weeks: NOEL<2.15 mg/kg, OECD 407 Dog oral, 13 weeks; NOEL=2.15 mg/kg, OECD 407 Damage is possible to: kidneys, eye, skin, gastrointestinal tract, reproductive organs (testicles, ovaries), breasts, spleen, pituitary, haematopoietic tissue
<b>Carcinogenic, Mutagenic/Genotoxic: and Reproductive Effects</b>	<u>Mutagenicity:</u> Micronucleus test, negative, mouse (male and female), oral <u>Genotoxicity, in vitro:</u> Ames test, Salmonella typhimurium, negative, EEC B 14 Cytogenetic test, in vitro, V 79 cells, negative, CECD In vitro, cytogenetic test (human lymphocytes), chromosomal aberration, negative <u>Reproduction Toxicity and Fertility:</u> Rat (male) oral: toxic effects on reproduction at 8.25 mg/kg. Rat (female) oral: toxic effects on reproduction and the foetus at 3.16 mg/kg
<b>Other Information</b>	none
<b>Practical Experience</b>	Symptoms: nausea, vomiting

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<b>12.</b>	<b>Information on Ecology</b>
	There are no available ecotoxicological studies. Information on a comparable product: miltefosin 1-0-hexadecylphosphocholine
<b>Persistence and Degradability</b>	Biological degradability Degradation (28 days), subject to slight degradation, OECD 301 E
<b>Mobility and Bioaccumulation Potential</b>	n.d.
<b>Ecotoxic Effects</b>	<i>Bacterial Toxicity</i> Pseudomonas putida, EC 10 (16 h) = 0.45 mg/l DEV, DIN 38412, T.8
<b>Other Damaging Effects</b>	<i>AOX Comment:</i> The product contains no organically bound halogen.
<b>Additional Ecological Comments</b>	<i>CSB Value:</i> Theoretical oxygen requirements (ThOD) = 2.53 gO <sub>2</sub> /g
	<i>BSB5 Value:</i> n.d.
	<i>According to the formulation, it contains the following heavy metals and compounds of EU Guidelines No. 76/464</i> n.a.
	<i>General Comments</i> none

<b>13.</b>	<b>Comments on Disposal</b>
<b>Product</b>	<i>Recommendation</i> The waste requires special monitoring and must be disposed of in accordance with local and national legal regulations.
	<i>Waste Key Number</i> No waste key number can be given for this product in accordance with the European Waste List (EAV) from the Waste List Regulation (AVV)), as classification is only possible on the basis of the use by the consumer. The waste key number must be awarded in agreement with the disposer / manufacturer / the authorities. Recommendation key number: 180108*
	<i>Waste Name</i> Can be burnt if local official regulations are respected.
<b>Uncleaned Packs</b>	<i>Recommendation</i> Can be burnt if the local official regulations are respected.

<b>14.</b>	<b>Information on Transport</b>
	Not a hazardous good in the sense of the transport regulations.

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<b>15.</b>	<b>Regulations</b>
<b>Labelling according to EU guideline</b>	<p><i>Labelled according to EU guideline</i></p> <p>Working labelling on the basis of own knowledge</p>
	<p><i>Letter Code and Risk Assessment of the Product</i></p> <p>T poisonous</p>
	<p><i>Component(s) Determining the Danger</i></p> <p>Perifosin (D-21266)</p> <p>4-[[Hydroxy(octadecyloxy)phosphinyl]oxy]-1,1-dimethylpiperidine, internal salt</p> <p>Caution: This substance has not yet been fully investigated.</p> <p>"Only for the professional user."</p>
	<p><i>R Code</i></p> <p>R 60-61-64-22-48/25</p> <p>Can impair reproductive ability.</p> <p>Can harm the foetus in the womb.</p> <p>Can harm babies through maternal milk.</p> <p>Harmful to health when swallowed.</p> <p>Poisonous: Risk of serious harm to health after protracted exposure from swallowing.</p>
	<p><i>S Code</i></p> <p>S 22-26-36/37/39-45-53</p> <p>Do not breathe in dust.</p> <p>After contact with the eyes, rinse immediately thoroughly with water and call for medical assistance.</p> <p>Wear suitable protective clothing, protective gloves and safety glasses/ facial protection.</p> <p>Call for medical assistance immediately if there is an accident or you feel unwell. If possible, show the doctor this label.</p> <p>Avoid exposure. Fetch specific instructions.</p>
<b>National regulations</b>	<p><i>Additional classification according to directive on hazardous goods</i></p> <p><i>Comments on restrictions to work with the material</i></p> <p>Pay attention to restrictions to work for expectant and nursing mothers.</p> <p>Pay attention to restrictions to work for adolescents.</p>
	<p><i>Regulation on Abnormal Function</i></p> <p>See appendix 1</p>
	<p><i>Classification according to VbF</i></p> <p>n.a.</p>
	<p><i>Technical Instruction for Air</i></p> <p>Figure: 5.2.7</p>
	<p><i>Water Risk Class (WGK):</i></p> <p>2, risk to water</p> <p>Classification according to VwVwS, Appendix 3</p> <p>These ecological data are based on analogies.</p>
	<p><i>Other Regulations, Restrictions and Regulations on Prohibition</i></p> <p>Caution: This substance has not yet been fully investigated.</p>

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	<p>According to paragraph 2 section 3 of the Chemicals Law, this product must be exclusively used for the production of drugs needing approval or registration in accordance with the Drug Law or the Law on Veterinary Diseases.</p> <p>VDI 2263 "Dust Fires and Dust Explosions; Risks, Assessments, Protective Measures."</p> <p>Storage in accordance with GefStoffV paragraph 24</p> <p>TRGS 525 "Work with hazardous substances in institutions for human medical care."</p> <p>Regulations for Protection at Work:</p> <p>Pay attention during work to BG leaflet M 050: "Work with substances presenting a health risk "</p> <p>Pay attention to work to BG leaflet M 057: "Safe work with hazardous substances in the pharmaceutical industry."</p> <p>Other countries: Pay attention to national regulations.</p>
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<b>16.</b>	<b>Other Information</b>
<b>Sources:</b>	<p><i>R Codes (Information in section 2)</i></p> <p>R 60: Can impair the reproductive ability.</p> <p>R 61: Can harm the foetus in the womb.</p> <p>R 64: Can harm babies through maternal milk.</p> <p>R 22: Can damage health when swallowed.</p> <p>R 48/25: Poisonous: Danger of severe harm to health after protracted exposure when swallowed.</p> <p>EU Guidelines            91/155/EEC (93/112/EU, 2001/58/EU)            67/548/EEC (2001/59/EU)            Regulation on Hazardous Substances (GefStoffV)            TRGS 200            TRGS 220            Water Balance Law (WHG)            Law on Recycling Economy and Waste (KRW-AbfG)            Guideline on Fire Water Retention (LöRüRL)</p>
	<p>The points marked with * have been changed from the last version.</p> <p>The above information corresponds to the current state of our knowledge and experience. On this basis, we wish to describe our product with respect to possible safety requirements. This is not intended as a guarantee of properties or a description of quality.</p>