SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

Contact information

General

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+1 (800) 424-9300 (USA and Canada)
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Product identifier

Thalomid® Capsules (50, 100, 150 and 200 mg)

Synonyms

For thalidomide: alpha-(N-Phthalimido)glutarimide; N(2,6-Dioxo-3-piperidyl)-phthalimide; 1H-Isoindole-1,3 (2H)-Dione, 2-(2,6-Dioxo-3-Piperidinyl)-

Trade names

Thalomid® Capsules

Chemical family

Piperidinedione (thalidomide)

Relevant identified uses of the substance or mixture and uses advised against

Bulk formulated pharmaceutical product/ Formulated pharmaceutical product packaged in final form for patient use

Note

The physical, chemical and ecological properties of this material and/or its ingredients have not been fully characterized. This SDS will be revisited as more data become available.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada. Please consult the prescribing/packaging information. **The classification and labelling listed below is for bulk Thalomid Capsules**.

Globally Harmonized System [GHS]

Reproductive Toxicity - Category 1A. Specific Target Organ Toxicity (repeated exposure) - Category 1.

SECTION 2 - HAZARDS IDENTIFICATION …continued

Label elements

GHS hazard pictogram

GHS signal word

Danger

GHS hazard statements

H360D - May damage the unborn child. H372 - Causes damage to hematological and neurological system through prolonged or repeated exposure.

GHS precautionary statements

P201 - Obtain special instructions before use. P260 - Do not breathe dust. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P281 - Use personal protective equipment as required. P308 + P313 - IF exposed or concerned: get medical advice/attention. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/ regional/national/international regulations.

Other hazards

Known human teratogen. A single dose of thalidomide taken by a pregnant woman can cause severe birth defects including limb defects (absent or shortened limbs) and facial abnormalities. Peripheral neuropathy (potentially severe and irreversible) has commonly been observed after repeated oral therapeutic doses of around 50 to 300 mg/day. An increased risk of thrombotic events including deep vein thrombosis and pulmonary embolus is associated with the therapeutic use of thalidomide, though concomitant therapy may be a contributing factor. Drowsiness, dizziness/orthostatic hypotension, rash and somnolence are the most commonly observed adverse events associated with the therapeutic use of thalidomide. Post-market reports of hypothyroidism, bowel obstruction and gastrointestinal perforations, sexual dysfunction, menstrual disorders (*e.g.*, amenorrhea), infections, convulsions, and heart attack (in patients with known risk factors) were also documented with therapeutic use.

Note

This mixture is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Starch	9005-25-8	232-679-6	50-60%	Not classified
Thalidomide	50-35-1	200-031-1	10-15%	STOT-R1; H372; RT1A: H360D

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS …continued

Note	The ingredient(s) listed above are considered hazardous. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications. Starch is included because it has OELs.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	Yes
Eye Contact	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.
Skin Contact	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
Inhalation	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
Ingestion	Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
Protection of first aid responders	See Section 8 for Exposure Controls/Personal Protection recommendations.
Most important symptoms and effects, both acute and delayed	See Sections 2 and 11.
Indication of immediate medical attention and special treatment needed, if necessary	Material is a formulated product that contains an immunomodulatory agent with antineoplastic and antiangiogenic properties. Contains a known teratogen. Potential neurological and blood toxicant. Medical conditions aggravated by exposure: A significantly increased risk of thrombotic events including deep vein thrombosis and pulmonary embolism is associated with therapeutic use of thalidomide, though concomitant therapy may be a contributing factor. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.

SECTION 5 - FIREFIGHTING MEASURES …continued

Specific hazards arising from the substance or mixture	No information identified. May emit toxic fumes of carbon monoxide, carbon dioxide, and oxides of nitrogen.
Flammability/ Explosivity	No information identified. High concentrations of finely divided organic particles can explode if ignited.
Advice for firefighters	Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	If material is released or spilled, cordon off spill area. Take proper precautions to minimize exposure by using appropriate personal protective equipment (see section 8). Area should be adequately ventilated. Do not breathe dust. Consider the use of appropriate respiratory protection.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	If capsules are broken or crushed, DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Add excess liquid to allow the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice.
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	If capsules are crushed or broken, dust containing drug substance may be released. Minimize dust generation and accumulation. Follow recommendations for handling bulk formulated/packaged pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Wash thoroughly after handling. Avoid breathing dust. Wash thoroughly after handling.
Conditions for safe storage including any incompatibilities	Store at room temperature away from incompatible materials. Keep out of reach of children. Avoid extreme temperatures. Protect from light. Store locked up.
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Starch	ACGIH, Belgium, Bulgaria, Portugal, Spain, Singapore	TWA-8 HR	10 mg/m³
	Czech Republic, Slovak Republic	TWA-8 HR	4 mg/m³
	Greece, NIOSH	TWA-8 HR	10 mg/m³ (inhalable fraction); 5 mg/m³ (respirable fraction)
	Ireland, United Kingdom	TWA-8 HR	10 mg/m³ (inhalable fraction); 4 mg/m³ (respirable fraction)
	OSHA	TWA-8 HR	15 mg/m³ (total dust); 5 mg/m³ (respirable fraction)
	United Kingdom	STEL	30 mg/m³ (inhalable fraction); 12 mg/m³ (respirable fraction)
	NIOSH	TWA-10 HR	10 mg/m³ (total dust); 5 mg/m³ (respirable fraction)
Thalidomide	Celgene	TWA-8 HR	0.5 µg/m³

DNELs/PNECs

None identified.

Exposure/Engineering controls

None required for normal handling of packaged product. If handling bulk capsules or capsules are crushed or broken: Control exposures to below the OEL (if available). Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Open handling should not be performed when handling potent substances, or substances of unknown toxicity. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

Respiratory protection

None required for normal handling of packaged product. If handling bulk capsules or capsules are crushed or broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly worn powered air-purifying respirator equipped with HEPA filters or combination filters should provide ancillary protection based on the known or foreseeable limitations of existing

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Respiratory protection …continued	engineering controls. Use a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where air purifying respirators may not provide adequate protection.
Hand protection	Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.
Skin protection	Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.
Eye/face protection	Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
Environmental Exposure Controls	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.
Other protective measures	Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	50-mg white opaque capsules; 100-mg tan capsules; 150-mg tan/blue capsules; 200-mg blue capsules
Color	White to off-white powder in capsules
Odor	No information identified.
Odor threshold	No information identified.
pH	No information identified.
Melting point/ freezing point	269-271°C (thalidomide)
Initial boiling point and boiling range	No information identified.
Flash point	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Evaporation rate	No information identified.
Flammability (solid, gas)	No information identified.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified.
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	<0.1 mg/mL (thalidomide)
Solvent solubility	No information identified.
Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

Molecular formula	Not applicable (Mixture)
Molecular weight	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Chemically stable; pharmacological stability not guaranteed beyond expiration date imprinted on package.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	Avoid extreme temperatures.
Incompatible materials	Strong oxidizers.

SECTION 10 - STABILITY AND REACTIVITY …continued

Hazardous decomposition products No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note **The following data describe the active ingredient, thalidomide.**

Information on toxicological effects

Route of entry May be absorbed by inhalation, skin contact and ingestion.

Acute toxicity

Compound	Type	Route	Species	Dose
Starch	--	--	--	--
Thalidomide	LD_{50}	Oral	Mouse	>5000 mg/kg
	LD_{50}	Oral	Rat	>3000 mg/kg (based on data from 14-day repeat-dose study)
	LD_{50}	Oral	Dog	>2000 mg/kg (based on data from 28-day repeat-dose study)

Irritation/Corrosion No data available.

Sensitization Thalidomide was negative in the mouse local lymph node assay.

STOT-single exposure No data available.

STOT-repeated exposure/Repeat-dose toxicity Dog, 28-day oral: No signs of significant toxicity at doses up to 2000 mg/kg/day.

Mouse, 90-day oral: Centrilobular hepatocellular hypertrophy was observed. NOAELs were 300 and <30 mg/kg/day for female and male mice, respectively.

Rat, 90-day oral: Decreased body weight with a dose response more evident in males. Decreases in platelet counts, total T3, total T4 and free T4, as well as changes in liver/kidney weights were observed. NOAEL was <30 mg/kg/day.

Dog, 53-week oral study: No mortality at doses up to 1000 mg/kg/day. Dose-dependent changes in clinical chemistry were observed. NOAEL was <43 mg/kg/day.

Reproductive toxicity Negative for fertility impairment in male and female rabbits treated orally with doses up to 500 and 100 mg/kg/day, respectively.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Developmental toxicity

Teratogenic effects have been seen in rabbits and monkeys at doses equal to or less than the human therapeutic dose. Teratogenicity has also been seen in rats and mice, but at higher doses.

In perinatal/postnatal oral toxicity studies, reduced viability was observed in rabbits treated with 150 and 500 mg/kg/day; the NOEL for pup viability and growth was 30 mg/kg/day. Additionally, a reduced pregnancy index and decreased fertility was observed in the F_1 generation at a maternal dose of 500 mg/kg/day. A dose-related increase of splayed limbs was also seen in the F_1 generation.

Genotoxicity

Negative in the Ames bacterial mutagenicity assay, a forward mutation assay in Chinese hamster ovary cells, a clastogenicity assay in cultured human lymphocytes and the *in vivo* micronucleus test in mice and rabbits.

Carcinogenicity

Negative in mice, male rats and female rats treated orally with doses up to 3000, 300, and 3000 mg/kg/day, respectively. Thalidomide is not listed by NTP, IARC, ACGIH or OSHA as a carcinogen.

Aspiration hazard

No data available.

Human health data

See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Starch	--	--	--
Thalidomide	LC_{50} (24-96 hours)	Fathead minnow	>1000 mg/L

Additional toxicity information

No EC_{50} (15-minute) was determined in the Microtox® assay at concentrations of thalidomide up to 45 mg/L.

Persistence and Degradability

Thalidomide is expected to be rapidly degraded during sewage and waste water treatment. It did not degrade in respirometry and sealed vessel CO_2 production tests.

Bioaccumulative potential

Based on a log K_{OW} of ~0.33-0.66, thalidomide would not be expected to bioaccumulate.

Mobility in soil

No data available.

Results of PBT and vPvB assessment

Not performed.

Other adverse effects

No data available.

Note

The environmental characteristics of the formulated product have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods	Dispose of wastes by appropriately permitted chemical waste incinerator in accordance to prescribed federal, state, and local guidelines. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, *e.g.*, appropriately permitted municipal or onsite wastewater treatment facility.

SECTION 14 - TRANSPORT INFORMATION

Transport	Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
UN number	None assigned.
UN proper shipping name	None assigned.
Transport hazard classes and packing group	None assigned.
Environmental hazards	Based on the available data, this product/mixture is not regulated as an environmental hazard or a marine pollutant.
Special precautions for users	Avoid release to the environment.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.
Chemical safety assessment	Not conducted.
TSCA status	Drugs are exempt from TSCA.
SARA section 313	Not listed.
California proposition 65	This product is or contains chemical(s) known to the state of California to cause developmental toxicity. (Thalidomide)

SECTION 15 - REGULATORY INFORMATION …continued

Additional information No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications RT1A - Reproductive toxicity Category 1A. STOT-R1 - Specific Target Organ Toxicity Following Repeated Exposure Category 1. H360D - May damage the unborn child. H372 - Causes damage to hematological and gastrointestinal systems through prolonged or repeated exposure.

Sources of data Information from published literature and internal company data.

Abbreviations ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System

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Revisions Minor formatting changes

Disclaimer The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be

Disclaimer …continued

used in the handling and use of the material because it is a potent pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.