SAFETY DATA SHEET

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

Contact information

General

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Product identifier	Idelalisib Tablets
Synonyms	GS-1101 Tablets
Trade names	Zydelig®
Chemical family	Mixture
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	This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product. 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 labeling listed below is for bulk Idelalisib® tablets and constituent ingredients.**
Globally Harmonized System [GHS]	Specific Target Organ Toxicity (repeated exposure) - Category 1.

Label elements

SECTION 2 - HAZARDS IDENTIFICATION …continued

GHS hazard pictogram

GHS signal word Danger

GHS hazard statements H372 - Causes damage to the immunological system through prolonged or repeated exposure.

GHS precautionary statements P260 - Do not breathe dust. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P314 - Get medical advice/ attention if you feel unwell. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.

Other hazards In patients with hematological malignancies, administration over a dose range of 50 mg/dose BID to 350 mg/dose BID and for periods >1 year was symptomatically well tolerated. Hematological laboratory abnormalities observed in clinical trials have included neutropenia, thrombocytopenia, anemia, and lymphopenia. Pneumonias and gastrointestinal inflammatory events (e.g., stomatitis, cecitis, diarrhea and colitis) have also been observed, as have increased levels of liver enzymes (ALT/AST). Additionally, rash has occurred following clinical administration of the drug orally.

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
Idelalisib	N/A	N/A	70-80%	STOT-RE1: H372
Cellulose	9004-34-6	232-674-9	10-12%	Not classified
Magnesium Stearate	557-04-0	209-150-3	1-2%	Not classified
Titanium dioxide	13463-67-7	236-675-5	0.8-0.9%	Not classified

Note The ingredient(s) listed above are considered hazardous. Cellulose, magnesium stearate, and titanium dioxide are listed because they have OELs. The remaining components are not hazardous and/or present at amounts below reportable limits. See Section 16 for full text GHS classifications. The GHS classifications are based on Regulation (EC) 1272/2008, WHMIS 2015 and Hazard Communication Standard No. 1910.1200.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	Yes
Eye Contact	In the event of a chemical exposure, immediately irrigate eyes with copious quantities of water for at least 15 minutes. Remove contact lenses as soon as practical. Do not delay irrigation while waiting for contact lens removal. 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	If swallowed, call a physician immediately. 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	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.
Specific hazards arising from the substance or mixture	No information identified. May emit carbon monoxide, carbon dioxide, oxides of nitrogen, fluorine-containing compounds, and/or magnesium-containing compounds.
Flammability/Explosivity	No explosivity or flammability data identified. High concentrations of finely divided airborne organic particles can potentially explode if ignited.
Advice for firefighters	In case of a fire, keep containers cool with water and remove from fire area. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Wash all equipment thoroughly after use. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated.

Environmental precautions Do not empty into drains. Avoid release to the environment.

Methods and material for containment and cleaning up If tablets are spilled, scoop up and dispose of in a manner that is compliant with federal, state or local laws. If tablets are crushed/broken, do not raise dust. Clean up spill with HEPA-filtered vacuum if available. If not available, add water to allow for the material to enter solution. Collect material with absorbents. Place spill materials into a leak-proof container suitable for disposal. Decontaminate area a second time. Dispose of material in a manner that is compliant with federal, state and local laws.

Reference to other sections See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling Follow recommendations for handling bulk formulated/packaged pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid contact with eyes, skin and other mucous membranes. Avoid breathing dust. Keep container tightly closed. Wash thoroughly after handling.

Conditions for safe storage including any incompatibilities Store between 20-30°C (68-86°F) with excursions permitted 15-30°C (59-86°F).

Specific end use(s) No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Idelalisib	Gilead	TWA-8 HR	20 µg/m
Cellulose	ACGIH, Australia, Belgium, Estonia, France, Portugal, Romania, Singapore, Spain	TWA-8 HR	10 mg/m

Control Parameters/Occupational Exposure Limit Values
…continued

Compound	Issuer	Type	OEL
Cellulose	Ireland, United Kingdom	TWA-8 HR	10 mg/m (inhalable dust); 4 mg/m (respirable dust)
	Ireland	STEL	20 mg/m (total inhalable dust)
	Latvia	TWA-8 HR	2 mg/m
	Mexico	TWA-8 HR/STEL	10/20 mg/m
	NIOSH	TWA-8 HR	10 mg/m (total dust); 5 mg/m (respirable dust)
	OSHA	TWA-8 HR	15 mg/m (total dust); 5 mg/m (respirable fraction)
	United Kingdom	STEL	20 mg/m (inhalable dust); 12 mg/m (respirable dust)
Magnesium Stearate	ACGIH	TWA-8 HR	10 mg/m (stearates)
	Lithuania	TWA-8 HR	3 mg/m
	Sweden	TWA-8 HR	5 mg/m
Titanium dioxide	ACGIH, Australia, Belgium, Bulgaria, Latvia, Poland, Portugal, Romania, Singapore, Spain, OSHA (vacated)	TWA-8 HR	10 mg/m
	Austria	TWA-8 HR	5 mg/m (respirable fraction)
	Austria	STEL (2 x 60 min)	10 mg/m (respirable fraction)
	Denmark	TWA-8 HR	6 mg/m (as Ti)
	Estonia, Lithuania, Sweden	TWA-8 HR	5 mg/m
	France, Mexico	TWA-8 HR	10 mg/m (as Ti)

Control Parameters/Occupational Exposure Limit Values
…continued

Compound	Issuer	Type	OEL
Titanium dioxide	Greece	TWA-8 HR	10 mg/m (inhalable fraction); 5 mg/m (respirable fraction)
	Ireland, United Kingdom	TWA-8 HR	10 mg/m (total inhalable dust); 4 mg/m (respirable dust)
	Mexico	STEL	20 mg/m (as Ti)
	NIOSH	IDLH	5000 mg/m
	Romania	STEL	15 mg/m
	United Kingdom	STEL	30 mg/m (total inhalable); 12 mg/m (respirable)

Exposure/Engineering controls
None required for normal handling of packaged product. If handling bulk tablets or tablets are crushed or broken: control exposures to below the OEL. Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at dust-generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling of powders. High-energy operations such as milling, particle sizing, spraying or fluidizing should be done within an approved emission control or containment system.

Respiratory protection
None required for normal handling of packaged product. If handling bulk tablets or tablets are crushed or broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine tablet handling tasks, an approved and properly fitted air-purifying respirator with HEPA filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a powered air-purifying respirator equipped with HEPA filters or combination filters or 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 a lower level of respiratory protection may not provide adequate protection.

Hand protection
Wear nitrile or other impervious gloves if skin contact is possible. 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.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

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 product, 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). Decontaminate all protective equipment following use.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Film-coated tablets
Color	Pink (150 mg) or Orange (100 mg)
Odor	No information identified.
Odor threshold	No information identified.
pH	Not applicable
Melting point/freezing point	No information identified.
Initial boiling point and boiling range	Not applicable
Flash point	No information identified.
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	No information identified.
Solvent solubility	No information identified..

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

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	No information identified.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Information on toxicological effects

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

Acute toxicity

Compound	Type	Route	Species	Dose
Idelalisib	Maximum Tolerated Dose	Oral	Rat	1500 mg/kg
	Maximum Tolerated Dose	Oral	Dog	25 mg/kg

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Acute toxicity
…continued

Compound	Type	Route	Species	Dose
Cellulose	LC_{50}	Inhalation	Rat	>5800 mg/m /4h
	LD_{50}	Oral	Rat	>5000 mg/kg
	LD_{50}	Dermal	Rabbit	>2000 mg/kg
Magnesium Stearate	LC_{50}	Inhalation	Rat	>2000 mg/m
Titanium dioxide	LD_{50}	Oral	Rat	>10000 mg/kg
	LD_{50}	Oral	Mouse	>10000 mg/kg
	LD_{50}	Dermal	Rabbit	>10000 mg/kg

Irritation/Corrosion No information identified.

Sensitization No information identified.

STOT-single exposure No information identified.

STOT-repeated exposure/Repeat-dose toxicity The NOAEL associated with repeat doses of idelalisib in 28-day and 13-week oral rat toxicity studies was 50 mg/kg/day, and following 26 weeks was 25 mg/kg/day. The NOAEL associated with repeat doses of idelalisib in 28-day and 13-week oral toxicity dog studies was 5 mg/kg/day, and following 39 weeks was <2.5 mg/kg/day. The target organs of toxicity in these studies were the lymphoid, liver, GI and male reproductive systems.

Reproductive toxicity Idelalisib did not adversely affect mating or fertility parameters after approximately 13 weeks of dosing at 100 mg/kg/day. The NOAEL for male systemic and reproductive organ toxicity of idelalisib was <25 mg/kg/day due to the organ weight changes, but the NOAEL for male fertility and reproductive performance was >100 mg/kg/day. In the female fertility study, 1 female in the 100 mg/kg/day group had a totally resorbed litter following dosing for 4 weeks. A relationship between idelalisib administration and the totally resorbed litter could not be determined. A dose level of 50 mg/kg/day was considered to be the NOAEL for early embryonic toxicity.

Developmental toxicity Idelalisib showed evidence of increased post-implantation loss, reduced fetal body weights, and teratogenicity in rats at maternally toxic doses ≥75 mg/kg/day. The NOAEL for embryo/fetal developmental toxicity was 25 mg/kg/day.

Genotoxicity Idelalisib was negative in a battery of short-term screening testing for genotoxicity, including the Ames assay, an *in vitro* chromosomal aberration test in human peripheral blood lymphocytes, and an *in vivo* rat micronucleus assay.

Carcinogenicity No studies identified. Titanium dioxide has been classified by the International Agency for Research on Cancer (IARC) as an IARC Group 2B carcinogen "possibly carcinogenic to humans". This classification is based upon animal inhalation studies. Epidemiology studies do not suggest an increased risk of cancer in humans from occupational exposure to titanium dioxide. None of the other components of this mixture present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.

Aspiration hazard No data available.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Human health data See "Section 2 - Other Hazards"

Additional information Mixture not yet fully tested.

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Idelalisib	--	--	--
Cellulose	--	--	--
Magnesium Stearate	--	--	--
Titanium dioxide	LC_{50}/48h	Leuciscus idus	>1000 mg/L

Persistence and Degradability No data available.

Bioaccumulative potential No data available.

Mobility in soil No data available.

Results of PBT and vPvB assessment No data available.

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 Used product should be disposed of according to local, state, and federal regulations. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site 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.

SECTION 14 - TRANSPORT INFORMATION …continued

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	Due to lack of data, 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	Not listed.
Additional information	No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	STOT-RE1 - Specific Target Organ Toxicity Following Repeat Exposure Category 1. H372 - Causes damage to the immunological system through prolonged or repeated exposure.
Sources of data	Information from published literature and internal company data.

SECTION 16 - OTHER INFORMATION …continued

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

Issue Date

2 February 2017

Revisions

This is the third version of this SDS.

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 used in the handling and use of the material because it is a 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.