SAFETY DATA SHEET

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

Contact information

General

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Product identifier

Niraparib Capsules

Synonyms

For niraparib: (S)-2-(4-(piperidin-3-yl)phenyl)-2H-indazole-7-carboxamide 4-methylbenzene sulfonate hydrate; (3S)-3-{4-[7-(Aminocarbonyl)-2H-indazol-2-yl]phenyl}piperidine (tosylate salt monohydrate); MK-4827; C-023971

Trade names

None identified

Chemical family

Mixture - contains an indazole

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

Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product/ mixture in form for patient use; under investigation for the treatment various cancers.

Note

This SDS is written to address potential worker health and safety issues associated with the handling of the active pharmaceutical mixture. The physical, chemical and ecological properties of this product/mixture 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. Consult prescribing/packaging information. **The classification and labeling listed below is for bulk drug product.**

Globally Harmonized System [GHS]	Acute Toxicity (Oral) Category 4. Germ Cell Mutagenicity - Category 2. Reproductive Toxicity - Category 2. Specific Target Organ Toxicity (repeated exposure) - Category 1.

Label elements

GHS hazard pictogram

GHS signal word	Warning
GHS hazard statements	H302 - Harmful if swallowed. H341 - Suspected of causing genetic defects. H361fd - Suspected of damaging fertility. Suspected of damaging the unborn child. H373 - May cause damage to bone marrow and lymphoid tissues through prolonged or repeated exposure.
GHS precautionary statements	P201 - Obtain special instructions before use. P260 - Do not breathe dust. 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. P264 - Wash hands 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.
Other hazards	Niraparib (administered as a tosylate monohydrate salt) is a potent PARP inhibitor that exerts antitumorigenic activity by disabling DNA repair mechanisms, thereby sensitizing cancer cells to other anticancer agents. Adverse effects noted with oral dosing in clinical trials were myelosuppression (anemia, thrombocytopenia, and neutropenia), gastrointestinal effects (nausea, vomiting, anorexia, and constipation), and fatigue. Based on its mechanism of action, potentials for increased infection and bruising, as well as for developmental and fertility effects cannot be excluded in the absence of definitive data.
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
Niraparib tosylate monohydrate	1613220-15-7	N/A	30-50 %	ATO4: H302; GCM2: H341; RT2: H361fd; STOT-R2: H373
Magnesium Stearate	557-04-0	209-150-3	<2 %	Not classified

Note The ingredient(s) listed above is considered hazardous. Magnesium stearate is listed because it has OELs and is present at or above 1%. The remaining components are not hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications.

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 Niraparib is a selective PARP inhibitor. Medical conditions aggravated by exposure: None reported. Treat symptomatically and supportively.

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 and sulfur, and other nitrogen- and sulfur-containing compounds.
Flammability/ Explosivity	No information identified.
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 capsules are opened/crushed/broken, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe dust.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	If capsules are spilled, scoop up and dispose of in a manner that is compliant with federal, state or local laws. If capsules are opened/crushed/broken, 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 into solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container 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 opened/crushed/broken, dust containing drug substance may be released. Minimize dust generation and accumulation. Follow recommendations for handling potent pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing dust. Wash thoroughly after handling.
Conditions for safe storage including any incompatibilities	Store at controlled room temperature (~20°C to 25°C), in a well-ventilated place with container tightly closed, away from incompatible materials. Avoid extreme temperatures. Protect from direct sunlight and moisture.
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note

Wash hands, face and other potentially exposed areas immediately in the event of physical contact.

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Niraparib tosylate monohydrate	Tesaro	8-hour TWA	2 μg/m^3
Magnesium Stearate	ACGIH	TWA-8 HR	10 mg/m^3 (stearates)
	Lithuania	TWA-8 HR	3 mg/m^3
	Sweden	TWA-8 HR	5 mg/m^3

Exposure/Engineering controls

None required for normal handling of packaged product. If handling bulk product and/or capsules are opened/crushed/broken: Control exposures to below the OEL for the active ingredient (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 product and/or capsules are opened/crushed/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 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

None required for normal handling of packaged product. Wear nitrile or other impervious gloves if skin contact with capsules is possible.

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

None required for normal handling of packaged product. Wear safety glasses with side shields if eye contact is likely, e.g., during clean up of large spill. Base the choice of protection on the job activity and potential for contact with eyes and face.

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.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

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	Powder in 2-part capsule
Color	Purple and white
Odor	No particular odor
Odor threshold	No information identified.
pH	Neutral (in 10% aqueous solution) (niraparib)
Melting point/ freezing point	Melts at 144 °C (niraparib)
Initial boiling point and boiling range	Not applicable.
Flash point	Not applicable.
Evaporation rate	Not applicable.
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	Very slightly soluble (niraparib)
Solvent solubility	Slightly Soluble in Acetone (niraparib) Soluble in DMF and Methyl Alcohol (niraparib) Freely Soluble in DMSO (niraparib)
Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Decomposition temperature	No information identified.
Viscosity	Not applicable.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

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

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable under normal handling and storage conditions.
Possibility of hazardous reactions	No information identified.
Conditions to avoid	Avoid extreme temperatures. Avoid direct sunlight and conditions that might generate heat.
Incompatible materials	Strong oxidizers, bases.
Hazardous decomposition products	See Section 5 - Hazardous combustion products.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note **No data on product formulation. The following information is for niraparib (the active ingredient) and other ingredients, where applicable.**

Information on toxicological effects

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

Acute toxicity

Compound	Type	Route	Species	Dose
Niraparib tosylate monohydrate	LD_{50}	Oral	Rat	<750 mg/kg (8-day study)
	Minimal Lethal Dose	Oral	Dog	>40.5 mg/kg (10-day study)
Magnesium Stearate	LC_{50}	Inhalation	Rat	>2000 mg/m^3

Irritation/Corrosion No studies identified.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Sensitization	No studies identified.
STOT-single exposure	No studies identified.
STOT-repeated exposure/Repeat-dose toxicity	In repeat-dose rat studies up to 90 days in duration, the primary treatment-related effects were mild bone/bone marrow toxicity that occurred at oral doses ≥30 mg/kg/day. With the exception of an increased amount of trabecula in the bone and minor arterial hypertrophy in the heart, all effects were reversible. A NOAEL of 10 mg/kg/day was identified. In repeat-dose dog studies up to 90 days in duration, the primary treatment-related effects were reversible hematological and spermatogenic effects that occurred at oral doses ≥12 and ≥6 mg/kg/day, respectively. A NOAEL of 4.5 mg/kg/day was identified.
Reproductive toxicity	No studies identified.
Developmental toxicity	No studies identified.
Genotoxicity	Niraparib tosylate monohydrate was negative in the Ames bacterial mutagenicity assay, although the hydrochloride salt yielded a positive result. Niraparib was also positive *in vitro* (an alkaline elution assay for DNA strand breaks in rat hepatocytes and chromosomal aberrations in Chinese hamster ovarian cells) and *in vivo* (rat bone marrow micronucleus assay).
Carcinogenicity	No studies identified. None of the components of the 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.
Human health data	See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Niraparib tosylate monohydrate	--	--	--
Magnesium Stearate	--	--	--

Persistence and Degradability	No data available.
Bioaccumulative potential	No data available.
Mobility in soil	No data available.

SECTION 12 - ECOLOGICAL INFORMATION …continued

Results of PBT and vPvB assessment	Not performed.
Other adverse effects	No data available.
Note	Ecological characteristics of this mixture were not available. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods	Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. 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 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.
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	RT2 - Reproductive toxicity Category 2. H361fd - Suspected of damaging fertility. Suspected of damaging the unborn child. ATO4 - Acute Toxicity (Oral) Category 4. H302 - Harmful if swallowed. GCM2 - Germ Cell Mutagenicity Category 2. H341 - Suspected of causing genetic defects. STOT-R2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2. H373 - May cause damage to bone marrow and lymphoid tissues 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

Issue Date	1 June 2016
Revisions	This is the first 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 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.