Safety Data Sheet

SECTION 1: Identification

Contact information

General

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Product identifier	Taletrectinib Capsules
Synonyms	Not applicable
Trade name	Not applicable
Chemical family	Mixture - contains an organic chemical
Recommended uses and restrictions	Bulk formulated pharmaceutical mixture OR Formulated pharmaceutical product/mixture packaged in final form for patient use; under investigation for the treatment of adult patients with advanced or metastatic non-small cell lung cancer (NSCLC) harbouring ROS1 mutations.
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product/mixture. Workers manufacturing this product/mixture should consult the SDS of each hazardous ingredient for hazard information and handling recommendations. This SDS will be revisited if more data become available.

SECTION 2: Hazard(s) identification

Classification of the substance or mixture The classification and labeling listed below is for bulk drug product.

Specific target organ toxicity – Repeated exposure, Category 2
May cause damage to organs (lungs, heart, gastrointestinal tract, lymphoid system, haematopoietic system) through prolonged or repeated exposure.

Label elements

GHS Hazard pictograms

GHS Signal word	Warning
GHS Hazard statements	H373 - May cause damage to organs (lungs, heart, gastrointestinal tract, lymphoid system, haematopoietic system) through prolonged or repeated exposure.
GHS Precautionary statements	P260 - Do not breathe dust. P314 - Get medical advice/attention if you feel unwell. P501 - Dispose of contents/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.
Other hazards	Taletrectinib is a small molecule anti-cancer agent, which inhibits the c-ros oncogene (ROS1) tyrosine-protein kinase and tropomyosin-receptor kinase (TRK). It is currently under investigation for oral administration in the treatment of adult patients with advanced or metastatic non-small cell lung cancer (NSCLC) harboring ROS1 mutations. Common treatment related adverse effects in clinical trials include increases in liver enzymes, diarrhea, nausea, vomiting and anemia.
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 number	EINECS/ELINCS#	Amount	GHS classification
Taletrectinib adipate	1505515-69-4	N/A	45 – 70 %	STOT RE 2, H373 (lungs, heart, gastrointestinal tract, lymphoid system, haematopoietic system)
Pregelatinized starch	9005-25-8	232-679-6	10 – 30 %	Not classified

Note The ingredient(s) listed above are considered hazardous. Pregelatinized starch is included because it has an OEL and is present at or above 1%. The remaining components are not hazardous and/or present at amounts below reportable limits. Amounts are listed as ranges; the exact percentage of composition is withheld as a trade secret. See Section 16 for full text of GHS classifications.

SECTION 4: First-aid measures

Description of first aid measures

Immediate medical attention and special treatment, if necessary Yes.

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.

Skin contact Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.

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.

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.

Most Important Symptoms/Effects Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively.

Expected Symptoms/Effects, Acute and Delayed See Sections 2 and 11.

SECTION 5: Fire-fighting measures

Suitable (and unsuitable) extinguishing media

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

Fire hazard No information identified.

Explosion hazard No information identified. High concentrations of finely divided organic particles can explode if ignited.

Special protective equipment and precautions for fire-fighters

Firefighting instructions In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

SECTION 6: Accidental release measures

Personal precautions, protective equipment and emergency procedures

Protective equipment 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.

Emergency procedures Do not breathe dust.

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

Methods and material for containment and cleaning up

Methods for 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 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. Scoop up broken pieces. 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 with an appropriate solvent (see section 9).

Other information Dispose of materials or solid residues at an authorized site.

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 potent 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. Wash thoroughly after handling. Do not breathe dust.

Conditions for safe storage, including any incompatibilities

Incompatible materials

Strong oxidizing agents.

Storage temperature

20 – 25 °C (with excursions permitted at 15 – 30°C)

Storage conditions

Store as directed by product packaging.

Specific end use(s)

Pharmaceuticals.

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 Limits

Name	Issuer	Value
Taletrectinib adipate	Nuvation Bio	*Consult manufacturer for details.
Pregelatinized starch	BE - Limit value [mg/m³]	10 mg/m³
	CH - VME [mg/m³]	3 mg/m³
	CZ - Expoziční limity (PEL) (mg/m³)	4 mg/m³
	ES - VLA-ED (mg/m³)	10 mg/m³
	IE - OEL (8 hours ref) (mg/m³)	10 mg/m³ total inhalable dust
	PT - OEL TWA (mg/m³)	10 mg/m³
	GB - WEL TWA (mg/m³)	10 mg/m³ inhalable aerosol
	ACGIH TWA (mg/m³)	10 mg/m³
	NIOSH REL TWA	10 mg/m³ (total dust)
	OSHA PEL TWA	15 mg/m³ (total dust)

Appropriate engineering controls

None required for normal handling of packaged product. If capsules are crushed or broken, or if handling bulk formulation: Control exposures to below the OEL (for the active ingredient(s) if available). Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. No open handling. Use specifically designed and engineered local exhaust ventilation (LEV) and/or enclosure at dust-generating points and for dust-generating operations unless process is contained. Isolation and closed containment technologies are strongly recommended (enclosed process - a barrier between the equipment and worker) with use of glove bags/continuous liners, isolator systems, direct connections and closed systems. Use clean-in-place systems.

Respiratory protection

None required for normal handling of packaged product. If capsules are crushed or broken, or if handling bulk formulation: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required when performing dust-generating operations. An airline respirator or self-contained breathing apparatus (SCBA) and disposable outerwear is required for spill cleanup.

Hand protection

None required for normal handling of packaged product. If capsules are crushed or broken, or if handling bulk formulation: 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.

Eye protection

None required for normal handling of packaged product. If capsules are crushed or broken, or if handling bulk formulation: 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.

Skin and body protection

None required for normal handling of packaged product. If capsules are crushed or broken, or if handling bulk formulation: Wear disposable coveralls appropriate to the task, booties, two pairs of gloves and safety glasses with side shields. Protective garments (coveralls, disposable coveralls, lab coats) are not to be worn in common areas (e.g., cafeterias) or out-of-doors. Employees must be trained in proper gowning and degowning practices. An anteroom or transition area must be used for gowning and degowning.

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).

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 9: Physical and chemical properties

Physical state

Solid

Appearance	Capsules
Formula	Mixture - not applicable
Molecular mass	Mixture - not applicable
Color	White to yellow
Odor	No data available
Odor threshold	No data available
pH	5.4
Melting point	178 – 183 °C
Freezing point	No data available
Boiling point	No data available
Flash point	No data available
Relative evaporation rate (butyl acetate=1)	No data available
Flammability (solid, gas)	No data available
Vapor pressure	No data available
Relative vapor density at 20°C	No data available
Relative density	No data available
Solubility	Slightly soluble in: methanol, dimethyl sulfoxide Water: 1.7 mg/ml
Log Pow	> 3.56 pH 10.8 buffer/n-octanol
Auto-ignition temperature	No data available
Decomposition temperature	No data available
Viscosity, kinematic	No data available
Viscosity, dynamic	No data available
Explosive limits	No data available
Explosive properties	No data available
Oxidizing properties	No oxidizing properties

SECTION 10: Stability and reactivity

Reactivity	The product is non-reactive under normal conditions of use, storage and transport.
Chemical stability	Stable under normal conditions.
Possibility of hazardous reactions	No dangerous reactions known under normal conditions of use.
Conditions to avoid	See section 7: Handling and Storage.
Incompatible materials	Strong oxidizing agents.
Hazardous decomposition products	Under normal conditions of storage and use, hazardous decomposition products should not be produced.

SECTION 11: Toxicological information

Note	No data on product formulation. The following information is for taletrectinib adipate and other ingredients, where applicable.
Likely routes of exposure	May be absorbed by inhalation, skin contact and ingestion.

Toxicological information

Acute toxicity

Component	Type	Dose
Pregelatinized starch	No data available	No data available
Taletrectinib adipate	No data available	No data available

Additional information	No data available
Serious eye damage/irritation	No data available
Skin corrosion/irritation	No data available
Sensitisation	No data available
STOT-single exposure	No data available
STOT-repeated exposure	Taletrectinib Rat (4-week), oral effect dose: 100 mg/kg/day Effects: Decreased body weight, spleen weight, reduced food consumption, changes in clinical pathology and clinical chemistry, and microscopic findings in striated muscle (e.g., heart, skeletal muscle), the renal tubular epithelium, and respiratory epithelium of the trachea. Rat (12-week), oral effect dose: 65 mg/kg/day Effects: Degeneration/necrosis in the heart and esophagus, microscopic changes

suggestive of systemic phospholipidosis (accumulation of a type of fat in cells throughout the body), and non-reversible microscopic findings in the lung (e.g., accumulation of foamy/vacuolated macrophages).

Monkey (4-week), oral, NOAEL: 10 mg/kg/day
Effect dose: 30 mg/kg/day
Effects: Dehydration, vomiting, reduction of body weight, changes in clinical pathology parameters, microscopic findings in the kidney, small intestine, mesenteric lymph nodes, and stomach.

Monkey (12-week), oral, NOAEL: 10 mg/kg/day
Effect dose: 30 mg/kg/day
Effects: Histopathological changes in the stomach and duodenum suggestive of irritant/inflammation response and microscopic changes suggestive of systemic phospholipidosis. At 60 mg/kg/day: mortality.

Reproductive toxicity

Taletrectinib
Rat (female), oral, NOAEL: 100 mg/kg/day
Effects: No effects on reproductive organs, number of ovarian corpora luteum, number of implants, number of live or dead foetuses, number of absorbed foetuses, mating index, pregnancy rate, or estrous cycle.

Rat (male), oral, NOAEL for fertility: 60 mg/kg/day
Effects: No effects on reproductive organs, fertility index, or sperm motility/count.

Developmental toxicity

Taletrectinib
Rat (embryofetal development), oral
Maternal NOAEL: 73.5 mg/kg/day (highest dose tested)
Fetal NOAEL: 22.1 mg/kg/day
Fetal effect dose: 73.5 mg/kg/day
Effects: Increased rate of abnormal ossification of the pelvic bone, considered related to taletrectinib.

Rabbit (embryofetal development), oral
Maternal NOAEL: 15 mg/kg/day
Maternal effect dose: 30 mg/kg/day
Fetal NOAEL: 90 mg/kg/day (highest dose tested)
Effects: Mortality/moribundity, and decreased food and water consumption.

Genotoxicity

Taletrectinib
In vitro:
Bacterial reverse mutation (Ames) Assay: negative
Chromosome aberration assay: positive

In vivo:
Rat micronucleus assay (bone marrow): negative
Rat micronucleus assay (liver): negative

Carcinogenicity

Carcinogenicity studies have not been conducted for taletrectinib adipate.

Silicon dioxide (7631-86-9)
Classified as carcinogenic to humans (IARC Group 1) in the form of quartz/cristobalite dust. Deemed to cause cancer of the lung in the form of quartz/cristobalite dust.

Aspiration hazard

No data available

Experience with humans

See "Section 2 - Other Hazards".

Other information

The toxicological properties of this mixture have not been fully characterized.

SECTION 12: Ecological information

Toxicity

Component	Type	Concentration
Pregelatinized starch	No data available	No data available
Taletrectinib adipate	No data available	No data available

Persistence and degradability

No data available

Bioaccumulative potential

No data available

Mobility in soil

No data available

Results of PBT assessment

No data available

Other adverse effects

No data available

Note

The environmental characteristics of this mixture 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. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines.

SECTION 14: Transport information

Transport	Based on the available data, this 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 class(es) (DOT)	None assigned.
Packing group	None assigned.
Marine pollutant	Based on the available data, this mixture is not regulated as an environmental hazard or a marine pollutant.
Special transport precautions	Avoid release to the environment.
Transport in bulk according to Annex II of Marpol 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	No chemical safety assessment has been carried out.
TSCA	Drugs are exempt from TSCA.
SARA Section 313 - Emission Reporting	This substance or mixture is not known to contain a toxic chemical or chemicals in excess of the applicable de minimis concentration as specified in 40 CFR §372.38(a) subject to the reporting requirements of section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 and 40 CFR Part 372.
California Proposition 65	California Proposition 65 - This product does not contain any substances known to the state of California to cause cancer, developmental and/or reproductive harm.
Additional information	No additional information available.

SECTION 16: Other information

Full text of H phrases and GHS classification	STOT RE 2 - Specific target organ toxicity – Repeated exposure, Category 2. H373 - May cause damage to organs through prolonged or repeated exposure.
Data sources	Information from published literature and internal company data.
Abbreviations and acronyms	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; PBT - Persistent, Bioaccumulative, and Toxic; 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; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System
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Indication of changes	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.