SAFETY DATA SHEETS

This SDS packet was issued with item:

078946727

The safety data sheets (SDS) in this packet apply to the individual products listed below. Please refer to invoice for specific item number(s).

078946722 078946725 078946726

Safety Data Sheet

SECTION 1: Identification

Contact information

General

Anivive Lifesciences Inc.
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Emergency telephone number + 1 (833) 264-8483 (24-hour availability)

Product identifier	Laverdia Tablets, 2.5 mg, 10 mg, and 50 mg
Synonyms	(Z)-3-[3-(3,5-Bis-trifluoromethylphenyl)-1H-[1,2,4]-triazol-1-yl]acrylic acid N'-pyridin-2-yl hydrazide, KY9, KPT-335, ALI-335, Verdinexor Tablets for Dogs.
Trade name	Laverdia
Chemical family	Mixture - contains acrylamide
Recommended uses and restrictions	Bulk formulated pharmaceutical mixture OR Formulated pharmaceutical product/mixture packaged in final form for veterinary use; indicated for the treatment of canine cancers.
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the mixture.

SECTION 2: Hazard(s) 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.

Reproductive toxicity Category 2
Suspected of damaging the unborn child.
Specific target organ toxicity (repeated exposure) Category 1
Causes damage to organs through prolonged or repeated exposure

Label elements

GHS Hazard pictograms

GHS Signal word Danger

GHS Hazard statements

H361d - Suspected of damaging the unborn child.

H372 - Causes damage to organs (thymus and testes) through prolonged or repeated exposure

GHS Precautionary statements

P201 - Obtain special instructions before use. P260 - Do not breathe dust. P264 - Wash hands, forearms and face thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P280 - Wear protective clothing, eye protection, face protection. P308+P313 - If exposed or concerned: Get medical advice/attention. P405 - Store locked up. P501 - Dispose of contents/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

Other hazards

Verdinexor is a selective inhibitor of nuclear export CRM1/XPO1 protein. Key clinical effects include headache, dizziness, lethargy, nausea, diarrhea, and sperm abnormalities.

CRM1/XPO1 protein has shown to be involved during normal embryonic development. As such, based on the mechanism of action, a potential for verdinexor to adversely affect embryonic development cannot be ruled out 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 number	EINECS/ELINCS#	Amount	GHS classification
Microcrystalline cellulose	9004-34-6	232-674-9	65 – 95 %	Not classified
Verdinexor	1392136-43-4	N/A	2.5 – 9.5 %	Repr. 2, H361d STOT RE 1, H372
Sodium lauryl sulfate	151-21-3	205-788-1	0.5 – 3.5 %	Flam. Sol. 2, H228 Acute Tox. 4 (Oral), H302 Acute Tox. 4 (Inhalation), H332 Skin Irrit. 2, H315 Eye Irrit. 2, H319 STOT SE 3, H335 Aquatic Chronic 3, H412
OPADRY	N/A	N/A	1 – 3 %	Not classified
Magnesium stearate	557-04-0	209-150-3	0.2 – 2 %	Not classified
Colloidal silicon dioxide	112945-52-5	231-545-4	0.5 – 1.5 %	Not classified

Note The ingredient(s) listed above are considered hazardous. The remaining components are not hazardous and/or present at amounts below reportable limits. Microcrystalline cellulose, colloidal silicon dioxide, and magnesium stearate are included because they have OELs and are present at or above 1%. Opadry (the coating material) is listed because it contains small amounts of titanium dioxide. Titanium dioxide is listed by IARC as a Group 2B Carcinogen (possibly carcinogenic to humans) and by ACGIH as A4 (not classifiable as a human carcinogen). However, these classifications are only applicable to the inhalation route of exposure. NTP determined that oral titanium dioxide was not carcinogenic. 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.

Specific hazards arising from the chemical No information identified. May emit carbon monoxide, carbon dioxide, oxides of fluorine and nitrogen and other fluorine- and nitrogen-containing compounds.

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 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. 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.

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

SECTION 7: Handling and storage

Precautions for safe handling — If tablets 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). Avoid contact with eyes, skin, and other mucous membranes. Wash thoroughly after handling. Do not breathe dust.

Conditions for safe storage, including any incompatibilities

Storage conditions — Keep container tight closed. Store locked up.

Storage temperature — 20 – 25 °C

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
Verdinexor	Anivive TWA	2 µg/m³
Microcrystalline cellulose	BE - Limit value [mg/m³]	10 mg/m³
	CH - VME [mg/m³]	3 mg/m³
	ES - VLA-ED (mg/m³)	10 mg/m³
	FR - VME [mg/m³]	10 mg/m³
	IE - OEL (8 hours ref) (mg/m³)	10 mg/m³ total inhalable dust
	IE - OEL (15 min ref) (mg/m3)	20 mg/m³ total inhalable dust
	LV - OEL TWA (mg/m³)	2 mg/m³
	PT - OEL TWA (mg/m³)	10 mg/m³
	GB - WEL TWA (mg/m³)	10 mg/m³ (inhalable aerosol)
	GB - WEL STEL (mg/m³)	20 mg/m³ (inhalable aerosol)
	ACGIH TWA (mg/m³)	10 mg/m³
	NIOSH REL (TWA) (mg/m³)	10 mg/m³ (total dust)
	OSHA PEL (TWA) (mg/m³)	15 mg/m³ (Total dust)
Magnesium stearate	ACGIH TWA (mg/m³)	10 mg/m³ (I - Inhalable particulate matter)
Colloidal silicon dioxide	AT - MAK [mg/m³]	4 mg/m³
	AU - TWA (mg/m³)	2 mg/m³
	CH - VME [mg/m³]	4 mg/m³
	ES - VLA-ED (mg/m³)	10 mg/m³
	FI - HTP-arvo (8h) (mg/m³)	5 mg/m³
	IE - OEL (8 hours ref) (mg/m³)	2.4 mg/m³
	DE - Occupational exposure limit value (mg/m³)	4 mg/m³
	GB - WEL TWA (mg/m³)	6 mg/m³ (inhalable aerosol)
	NIOSH REL (TWA) (mg/m³)	6 mg/m³
	OSHA PEL (TWA) (mg/m³)	80 mg/m³ (per % silica total dust)
	OSHA PEL (TWA) (ppm)	20 mppcf
Sodium lauryl sulfate	No data available	No data available
OPADRY	No data available	No data available

Appropriate engineering controls	None required for normal handling of packaged product. If tablets 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 tablets 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 tablets 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 tablets 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 tablets 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	Tablets
Formula	Mixture - not applicable
Molecular mass	Mixture - not applicable
Color	Orange – 2.5 mg; Light blue – 10 mg; Green – 50 mg
Odor	No data available
pH	No data available
Melting point	119.5 – 123.2 °C (for verdinexor)
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	For verdinexor: Sparingly soluble in ethanol. Soluble in DMSO
Water solubility	For verdinexor: Insoluble
Log Kow	No data available
Auto-ignition temperature	No data available
Decomposition temperature	No data available
Viscosity, kinematic	No data available
Viscosity, dynamic	No data available
Explosion limits	No data available
Explosive properties	No data available
Oxidizing properties	No data available

SECTION 10: Stability and reactivity

Reactivity	No information available.
Chemical stability	Not established.
Possibility of hazardous reactions	No data available.
Conditions to avoid	(See section 7: Handling and Storage).
Incompatible materials	No information available.
Hazardous decomposition products	None known.

SECTION 11: Toxicological information

Note	No data on product formulation. The following information is for verdinexor and other ingredients, where applicable.
Likely routes of exposure	None likely for packaged product. Tablets and or crushed/broken tablets and bulk material may be absorbed by inhalation, skin contact and ingestion.

Toxicological information

Acute toxicity

Component	Type	Dose
Verdinexor	No data available	No data available
Microcrystalline cellulose	LD50 oral rat	> 5 g/kg
	LD50 dermal rabbit	> 2 g/kg
	LC50 Inhalation - Rat	> 5800 mg/m³ (4hr)
Magnesium stearate	LD50 oral rat	> 10000 mg/kg
	LC50 Inhalation - Rat	> 2000 mg/m³
Colloidal silicon dioxide	LD50 oral rat	3160 mg/kg
Sodium lauryl sulfate	LD50 oral rat	1288 mg/kg
	LD50 dermal rabbit	mg/kg Min: 2000 Max: 20000
	LC50 Inhalation - Rat	> 3.9 mg/l
OPADRY	No data available	No data available

Serious eye damage/irritation	In rabbits, sodium lauryl sulfate is an eye irritant.
Skin corrosion/irritation	In rabbits, sodium lauryl sulfate is a skin irritant.
Sensitization	No data available
STOT-single exposure	No data available
STOT-repeated exposure	Oral administration of verdinexor in dogs at doses 1-1.75 mg/kg/dose (administered three times a week) for 13 weeks resulted in inappetence, thin body condition, excessive shedding, and decreased body weight and changes in blood parameters and clinical chemistry. Target organs of toxicity were male reproductive organs (e.g., atrophy/degeneration of seminiferous tubules), and thymus (lymphoid depletion). Oral administration in monkeys at doses 1-4 mg/kg/dose (administered four times in two weeks) was associated with body weight losses (~8%) and clinical pathology changes (lower hematocrit and phosphorus values) were noted at 4 mg/kg/dose.
Reproductive toxicity	Oral NOAELs for verdinexor for reproductive performance/fertility in rats were reported as 10 and 15 mg/kg/dose in males and females, respectively (administered twice per week). Additional details from these studies were not identified.
Developmental toxicity	No detailed studies with verdinexor were identified. Embryo/fetal developmental study on structurally- and mechanistically-similar compound in rats showed maternal and fetal toxicities (lower fetal weights and skeletal variations) at fairly low oral doses.
Genotoxicity	Verdinexor was not mutagenic in the Ames bacterial reverse mutation assay. It was also negative in an in vitro chromosome aberration assay in human peripheral blood leukocytes and in vivo micronucleus assay in rats.
Carcinogenicity	No data available for verdinexor. Titanium dioxide is listed by IARC as a Group 2B Carcinogen (possibly carcinogenic to humans) and by ACGIH as A4 (not classifiable as a human carcinogen). However, these classifications are only applicable to the inhalation route of exposure. NTP determined that oral titanium dioxide was not carcinogenic. 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
Experience with humans	See "Section 2 - Other Hazards".

SECTION 12: Ecological information

Toxicity

Component	Type	Concentration
Verdinexor	No data available	No data available
Microcrystalline cellulose	No data available	No data available
Magnesium stearate	No data available	No data available
Colloidal silicon dioxide	No data available	No data available
Sodium lauryl sulfate	LC50 fish	< 29 mg/l
	LC50 fish	4.1 mg/l
	EC50 crustacea	3.15 mg/l
	EC50 Daphnia	5.55 mg/l
	ErC50 (algae)	> 120 mg/l
OPADRY	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, 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 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 other information identified.

SECTION 16: Other information

Full text of H phrases and GHS classification	Acute Tox. 4 (Inhalation) - Acute toxicity (inhalation) Category 4. Acute Tox. 4 (Oral) - Acute toxicity (oral) Category 4. Aquatic Chronic 3 - Hazardous to the aquatic environment - Chronic Hazard Category 3. Eye Irrit. 2 - Serious eye damage/eye irritation Category 2. Flam. Sol. 2 - Flammable solids Category 2. Repr. 2 - Reproductive toxicity Category 2. Skin Irrit. 2 - Skin corrosion/irritation Category 2. STOT RE 1 - Specific target organ toxicity (repeated exposure) Category 1. STOT SE 3 - Specific target organ toxicity (single exposure) Category 3. H228 - Flammable solid. H302 - Harmful if swallowed. H315 - Causes skin irritation. H319 - Causes serious eye irritation. H332 - Harmful if inhaled. H335 - May cause respiratory irritation. H361d - Suspected of damaging the unborn child. H372 - Causes damage to organs through prolonged or repeated exposure. H412 - Harmful to aquatic life with long lasting effects.
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
Issue date	27 October 2020
Current revision	1.0
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.