SAFETY DATA SHEET

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

Contact information

General

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Product identifier	Telotristat Etiprate Coated Tablets (250 mg)
Synonyms	For telotristat etiprate: (S)-Ethyl 2-amino-3-(4-(2-amino-6-((R)-1-(4-chloro-2-(3-methyl-1H-pyrazol-1-yl)phenyl)-2,2,2-trifluoroethoxy)pyrimidin-4-yl)phenyl)propanoate 2-benzamidoacetate; L-Phenylalanine, 4-[2-amino-6-[(1R)-1-[4-chloro-2-(3-methyl-1H-pyrazol-1-yl)phenyl]-2,2,2-trifluoroethoxy]-4-pyrimidinyl]-, ethyl ester, compd. with N-benzoylglycine (1:1); LX1606 Hippurate; LP-778914-03
Trade names	Xermelo™
Chemical family	Mixture - contains a phenylalanine derivative
Relevant identified uses of the substance or mixture and uses advised against	Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product/ mixture for research and development; under investigation for use in the treatment of carcinoid syndrome (CS).
Note	The pharmacological, toxicological, and ecological properties of this product/ mixture have not been fully characterized. This data sheet will be updated as more data become available.

SECTION 2 - HAZARDS IDENTIFICATION

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

SECTION 2 - HAZARDS IDENTIFICATION …continued

Globally Harmonized System [GHS]	Mixture not yet fully tested.
Other/Supplemental	Hazard Not Otherwise Classified (US OSHA).

Label elements

GHS hazard pictogram	None required
GHS signal word	None required
GHS hazard statements	None required
GHS precautionary statements	None required
Other hazards	Telotristat etiprate is a tryptophan hydroxylase (serotonin-synthesizing enzyme) inhibitor under investigation for the treatment of CS. Oral doses used in clinical trials have ranged from 500-1,500 mg/day. The most commonly reported adverse effects seen to date were mild to moderate gastrointestinal (GI) effects, fatigue, and taste disturbances.
US Signal word	Caution
US Hazard overview	Contains telotristat etiprate - a tryptophan hydroxylase inhibitor. Mixture not yet fully tested. Combustible dust.
Note	This mixture does not meet criteria for classification according to directive 1999/45/EC and Regulation EC No 1272/2008 (EU CLP). Nevertheless, it should be regarded as hazardous because it has not yet been full tested and it contains a pharmacologically active ingredient. See Section 16 for full text of EU and GHS classifications.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Telotristat Etiprate	1137608-69-5	N/A	56.2 %	Not Classified
Cellulose	9004-34-6	232-674-9	5 %	Not classified

Note The ingredients listed above are considered hazardous and/or are pharmacologically active. Cellulose (as hydroxypropyl cellulose) is included because it has OELs and is present at or above 1%. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of EU and 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	Contains telotristat etiprate - a tryptophan hydroxylase inhibitor. Medical conditions aggravated by exposure: None known or 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. Combustion products may include carbon monoxide, carbon dioxide, oxides of nitrogen, hydrogen chloride and other chlorine- and fluorine-containing compounds.
Flammability/ Explosivity	For telotristat etiprate: Class 2 combustible dust: Kst 298 bar.m/s; Minimum Ignition Energy 10-25 mJ; Minimum Ignition Temperature 500-510 °C; limiting oxygen concentration 9-10% by volume.
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 tablets are crushed or 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 tablets are spilled, scoop up and dispose of in a manner that is compliant with federal, state or local laws. If tablets are crushed or 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 with an appropriate solvent (see Section 9).
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 pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing dust. Wash thoroughly after handling. Avoid contact with eyes, skin and clothing. Do not permit eating/drinking/ smoking near this material.
Conditions for safe storage including any incompatibilities	Keep in tightly sealed containers in a well-ventilated area. Store at 25 °C with excursions permitted to 15 °C to 30 °C. Keep away from incompatible materials. Avoid extreme temperatures.
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
Telotristat Etiprate	Lexicon	Occupational Exposure Limit (OEL)	1 mg/m³ (DRAFT)

Control Parameters/ Occupational Exposure Limit Values

…continued

Compound	Issuer	Type	OEL
Cellulose	ACGIH, Australia, Belgium, Estonia, France, Portugal, Romania, Singapore, Spain	TWA-8 HR	10 mg/m³
	Ireland, United Kingdom	TWA-8 HR	10 mg/m³ (inhalable dust); 4 mg/m³ (respirable dust)
	Ireland	STEL	20 mg/m³ (total inhalable dust)
	Latvia	TWA-8 HR	2 mg/m³
	Mexico	TWA-8 HR/STEL	10/20 mg/m³
	NIOSH	TWA-8 HR	10 mg/m³ (total dust); 5 mg/m³ (respirable dust)
	OSHA	TWA-8 HR	15 mg/m³ (total dust); 5 mg/m³ (respirable fraction)
	United Kingdom	STEL	20 mg/m³ (inhalable dust); 12 mg/m³ (respirable dust)

Exposure/Engineering controls

If tablets are crushed/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

If tablets are 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 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.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Hand protection	None required for normal handling. Wear nitrile or other impervious gloves if skin contact with tablets 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	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	Tablets
Color	White to off-white
Odor	No information identified.
Odor threshold	No information identified.
pH	No information identified.
Melting point/ freezing point	No information identified.
Initial boiling point and boiling range	No information identified.
Flash point	No information identified.
Evaporation rate	Not applicable.
Flammability (solid, gas)	No information identified.
Upper/lower flammability or explosive limits	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

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.
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 weight	Not applicable (Mixture)
Molecular formula	Not applicable (Mixture)
Other	No information identified.

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable under recommended storage conditions.
Possibility of hazardous reactions	No information identified.
Conditions to avoid	Protect from moisture.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note	**The following data describe the active ingredient and/or the individual 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
Telotristat Etiprate	LD_{50}	Oral	Rat	>2000 mg/kg
Cellulose	LC_{50}	Inhalation	Rat	>5800 mg/m³/4h
	LD_{50}	Oral	Rat	>5000 mg/kg
	LD_{50}	Dermal	Rabbit	>2000 mg/kg

Irritation/Corrosion In an acute dermal irritation/corrosion study conducted in New Zealand White Rabbits, telotristat etiprate was found not to be a dermal irritant.

Sensitization No data available.

STOT-single exposure In a single dose study in rats, telotristat etiprate caused transient alterations in stool character and minor, reversible effects on clinical pathology test results at 2000 mg/kg; effects were not considered adverse. Thus, the NOAEL in rats for a single dose of telotristat etiprate is 2000 mg/kg.

STOT-repeated exposure/Repeat-dose toxicity In a 26 week study using rats, a NOAEL of 50 mg/kg/day for telotristat etiprate was identified. This was based on effects of the compound on the glandular and non-glandular stomach. At 500 mg/kg/day, mean body weight was reduced (relative to controls) and mean body weight change was decreased in males. There were no clinically significant adverse effect on clinical chemistry, hematology, or urinalysis. All effects were reversible.

In a 39-week study using dogs, a NOAEL of 300 mg/kg/day was identified for telotristat etiprate. Although minor clinical signs (alterations in stool character) and minimal changes in clinical pathology were noted at doses of 150 and 300 mg/kg/day, these effects reversed with recovery and were not considered adverse.

Reproductive toxicity Telotristat etiprate did not adversely affect fertility and reproductive performance in rats, at oral doses up to 500 mg/kg/day. It had no effect on pre- and post-natal development, including maternal function, in the rat at oral doses up to 500 mg/kg/day.

Developmental toxicity In the rat, the no-effect levels for maternal toxicity and embryo-fetal toxicity with telotristat etiprate are 500 and 750 mg/kg/day, respectively. In the rabbit, the NOAEL for maternal toxicity is 125 mg/kg/day; the no effect level for embryo-fetal viability is 125 mg/kg/day, the no effect level for embryo-fetal growth is 250 mg/kg/day, and the no effect level for embryo-fetal development is 500 mg/kg/day.

Genotoxicity Telotristat etiprate was not genotoxic in an Ames bacterial mutagenicity assay, *in vitro* chromosomal aberration assays in cultured Chinese hamster ovary cells and human lymphocytes, and an *in vivo* rat bone marrow micronucleus test.

Carcinogenicity In a 26-week study in hemizygous Tg.rasH2 mice, telotristat etiprate did not increase the incidence of neoplastic lesions.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Aspiration hazard No data available.

Human health data See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Telotristat Etiprate	--	--	--
Cellulose	--	--	--

Persistence and Degradability No data available.

Bioaccumulative potential No data available.

Mobility in soil No data available.

Results of PBT and vPvB assessment Not performed.

Other adverse effects Not expected to undergo photolysis (telotristat etiprate).

Note Ecological characteristics of this mixture were not available. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods Product should be disposed of according to applicable local waste disposal 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 with prescribed local guidelines. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe and compliant manner (see Sections 6 and 8).

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 classes and packing group None assigned.

SECTION 14 - TRANSPORT INFORMATION …continued

Environmental hazards	Based on the available data, this mixture is not regulated as an environmental hazard or a marine pollutant.
Special precautions for users	No special precautions needed.
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.
WHMIS classification	Combustible dust - Category 1
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 R phrases and EU Classifications	Not applicable.
Full text of H phrases and GHS classifications	Not applicable.
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

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued	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; 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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