Safety Data Sheet

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

Theravance Biopharma US, Inc. 901 Gateway Blvd South San Francisco, CA 94080 Main: 650-808-6000 Fax: 650-808-4069 E-mail: SDS@theravance.com		**Emergency telephone number: Chemtrec +1 (800) 424-9300 (USA and Canada) +1 (703) 527-3887 (Collect calls accepted)**
Product identifier		Telavancin Hydrochloride - Lyophilized powder for injection
	Synonyms	None identified
	Trade names	VIBATIV®
	Chemical family	Mixture containing a lipoglycopeptide antibiotic.
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. Used as an antibiotic.
Note		This SDS is written to address potential worker health and safety issues associated with the handling of the formulated drug product.
Issue Date		12 June 2014

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 VIBATIV®.
	Regulation (EC) 1272/2008 [GHS]	Reproductive Toxicity - Category 2.
	Directive 67/548/EEC or 1999/45/EC	Xn: R63 (Repr. Cat 3).

SECTION 2 - HAZARDS IDENTIFICATION (continued)

Label elements		
	CLP/GHS hazard pictogram	
	CLP/GHS signal word	Warning
	CLP/GHS hazard statements	H361d – Suspected of damaging the unborn child.
	CLP/GHS precautionary statements	P201 - Obtain special instructions before use. P202 - Do not handle until all safety precautions have been read and understood. 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.
	EU symbol/indication of danger	 Xn - Harmful
	Risk (R) Phrase(s)	R63 - Possible risk of harm to the unborn child.
	Safety Advice	S2 - Keep out of reach of children. S7 - Keep container tightly closed. S29 - Do not empty into drains. S46 - If swallowed, seek medical advice immediately and show this container or label. S53 - Avoid exposure - Obtain special instructions before use.
Other hazards		In human clinical trials, the most common adverse reactions associated with clinical doses of telavancin included: taste disturbance, nausea, vomiting, and foamy urine. Additionally, telavancin may cause QTc prolongation at clinical doses. Effects on the kidney (e.g., increase in serum creatinine) and diarrhea that is typically associated with use of an antibacterial may also occur from treatment.
US Signal word		Caution
US Hazard overview		Contains telavancin hydrochloride - an antibacterial agent. Possible developmental hazard - may cause adverse effects in the developing fetus (based on animal data).
Note		This product/mixture is classified as dangerous/hazardous according to Directive 1999/45/EC, Regulation EC No 1272/2008 (EU CLP) and applicable US regulations. See Section 16 for full text of EU and GHS classifications. The CLP/GHS classifications are based on Regulation (EC) 1272/2008. The EU symbol/indicator of danger, R Phrases and Safety Advice are based on Directive 1999/45/EC.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ELINCS#	Amount	EU Classification	GHS Classification
Telavancin Hydrochloride	560130-42-9	N/A	7-9%	Harmful - Xn: R63	RT2: H361d
Note	The ingredients listed above are considered hazardous. 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. The EU classification is based on Directive 67/548/EEC and the CLP/GHS classification is based on Regulation (EC) 1272/2008.				

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	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	Medical conditions aggravated by exposure: None known or reported. 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 toxic fumes of carbon monoxide and carbon dioxide, oxides of nitrogen, and phosphorus-containing compounds.
Flammability/ Explosivity	No explosivity or flammability data identified. High airborne concentrations of finely divided organic particles can potentially explode if ignited.
Advice for firefighters	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.

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	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	Follow recommendations for handling 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. Avoid breathing dust.
Conditions for safe storage including any incompatibilities	Store original packages at refrigerated temperatures of 2 to 8°C (35 to 46 °F). Excursions to ambient temperatures (up to 25 °C (77 °F) are acceptable. Avoid excessive heat.
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/Occupational Exposure Limit Values			
Compound	**Issuer**	**Type**	**OEL**
Telavancin Hydrochloride	Theravance Biopharma US, Inc.	TWA-8 HR	600 µg/m³

Exposure/Engineering controls	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	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.
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.
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). Decontaminate all protective equipment following use.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties		
	Appearance	Lyophilized powder
	Color	White to slightly colored
	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.
	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)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	Avoid excessive heat.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note		**The following data describe the active ingredient, telavancin hydrochloride.**			
Information on toxicological effects					
	Route of entry	May be absorbed by inhalation, skin contact and ingestion.			
	Acute toxicity				
	Compound	**Type**	**Route**	**Species**	**Dose**
	Telavancin Hydrochloride	Minimum Lethal Dose	Intravenous (bolus)	Mouse	100 mg/kg
		Minimum Lethal Dose	Intravenous (bolus)	Rat (male)	100 mg/kg
		Minimum Lethal Dose	Intravenous (bolus)	Rat (female)	>150 mg/kg
	Irritation / Corrosion	Although some ocular irritation was noted in rabbits in the first day after ocular application of telavancin (API), due to the transient nature and reversibility of the changes, telavancin was not classified as an eye irritant. There was no evidence of skin irritation in rabbits after dermal application of telavancin (API) and the compound is classified as a non-irritant.			
	Sensitization	No studies identified.			
	STOT-single exposure	No studies identified.			
	STOT-repeated exposure/Repeat-dose toxicity	In a four week study in rats, doses of 50 mg/kg/day telavancin were associated with increased levels of blood urea nitrogen (BUN) and creatinine. Renal tubular degeneration, renal tubular vacuolation, and urothelial cell vacuolation were also observed. These effects occurred at a drug exposure similar to those measured in clinical trials. In a four-week study in dogs using 50 mg/kg/day telavancin, infusion-related (hypersensitivity) reactions during the first week of dosing were seen. Pathologic changes were confined to multifocal bilateral renal (cortical) tubular dilatation. Renal tubular vacuolation and renal tubular degeneration/necrosis were also present, as well as vacuolation of the urothelium of the renal pelvis and urinary bladder.			

SECTION 11 - TOXICOLOGICAL INFORMATION (continued)

	STOT-repeated exposure/Repeat-dose toxicity (continued)	In a 13-week study in rats at doses of 50 and 100 mg/kg/day, the primary target organs of toxicity were the liver and kidneys, as characterized by hepatocyte degeneration and proximal tubular degeneration. A 13-week study in dogs resulted in infusion-related reactions during the first three weeks of dosing with 50 and 100 mg/kg/day. Hepatocellular degeneration/necrosis, as well as, increases in liver enzymes and BUN and creatinine were also reported. Macrophage vacuolation in a variety of tissues and organs, including the kidneys, prostatic urethra and urinary bladder, and epididymides was noted. In a 26- week study in rats, lower red blood cell (RBC) counts, hemoglobin, and hematocrit, as well as increased BUN, creatinine and liver enzymes were seen.
	Reproductive toxicity	Telavancin did not affect the fertility or reproductive performance of adult male rats (exposed to telavancin for at least 4 weeks prior to mating) or female rats (exposed to telavancin for at least 2 weeks prior to mating). Male rats given telavancin for six weeks, at exposures similar to those measured in clinical studies, displayed altered sperm parameters that were reversible following an eight-week recovery period.
	Developmental toxicity	In embryo-fetal development studies in rabbits, minipigs, and rats, telavancin demonstrated the potential to cause limb and skeletal malformations when given intravenously during the period of organogenesis at doses up to 45, 75, and 150 mg/kg/day, respectively. Malformations in individual animals considered as potentially related to treatment included short limbs (rats and rabbits) and fused, missing, and/or too many toes (rats, minipigs, and rabbits). Flexed front paw and absent ulna (rabbits), and deformed front leg (minipigs) were also noted. Fetal body weights were decreased in rats. In a prenatal/perinatal development study, pregnant rats received intravenous telavancin at up to 150 mg/kg/day from the start of organogenesis through lactation. Offspring showed decreases in fetal body weight and an increase in the number of stillborn pups, along with one pup showing limited use of one limb for a few days.
	Genotoxicity	Telavancin was negative in a battery of short-term screening tests for genotoxicity, including: Ames bacterial cell mutagenicity assay, an *in vitro* chromosome aberration assay in human lymphocytes, and an *in vivo* mouse micronucleus assay.
	Carcinogenicity	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**
	Telavancin Hydrochloride	--	--	--

SECTION 12 - ECOLOGICAL INFORMATION (continued)

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	Ecological characteristics of this product/mixture were not available. 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.
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 complies with the requirements under US, EU and GHS (EU CLP - Regulation EC No 1272/2008) guidelines. Consult your local or regional authorities for more information.
Chemical safety assessment	Not conducted.
OSHA Hazardous	**Drugs packaged in their finished state and intended for final users are not subject to labeling in the US or under GHS.** If handling the bulk formulation, the following labels apply: Yes. Caution. Possible developmental toxicant - may cause harm to the developing fetus (based on animal data).
WHMIS classification	Not required. Drugs are not subject to WHMIS. This product/mixture has been classified in accordance with the hazard criteria of the Controlled Products Regulations and the SDS contains all of the information required by those regulations.
TSCA status	Drugs are exempt from TSCA.
SARA section 313	Not listed.
California proposition 65	Not listed.

SECTION 16 - OTHER INFORMATION

Full text of R phrases and EU Classifications	Xn - Harmful. R63 - Possible risk of harm to the unborn child.
Full text of H phrases, P phrases and GHS classification	Reproductive toxicity Category 2. H361d - Suspected of damaging the unborn child.
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, Labeling, 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; 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
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 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.