Safety Data Sheet

Date: 03-April-2023 **Luxturna (**Voretigene neparvovec-rzyl)

The information contained herein is not intended for therapeutic or patient use. For other applications, the information provided is believed to be complete and accurate at the time of issue. This document provides occupational health, safety, and environmental data applicable in manufacturing, industrial and workplace settings. It is not a specification sheet and none of the displayed data or lack of data should be construed as a specification. Roche and Spark Therapeutics assume no liability or responsibility resulting from the use or reliance on this information.

SECTION 1: Identification

Contact information

General

Spark Therapeutics, Inc.
3737 Market Street, Suite 1300
Philadelphia, PA 19104 USA
T 1-855-SPARKTX

Emergency telephone number

For Hazardous Materials [or Dangerous Goods] Incident: Spill, Leak, Fire, Exposure, or Accident
Call CHEMTREC®
USA and Canada: 1-800-424-9300 CCN 1010675
Outside the USA: +1-703-527-3887

Product identifier	Voretigene neparvovec
Synonyms	Voretigene neparvovec-rzyl; AAV2-hRPE65v2 ; Synthetic adeno-associated virus 2 vector AAV2-hRPE65v2
Trade name	LUXTURNA®
Chemical family	Recombinant adeno-associated virus 2 (AAV2) vector
Recommended uses and restrictions	Bulk formulated pharmaceutical product OR Formulated pharmaceutical product packaged in final form for patient use; indicated for the treatment of patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy and viable retinal cells as determined by the treating physician(s).
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the specified product.

SECTION 2: Hazard(s) identification

Classification of the substance or mixture

Not classified

Label elements

GHS Hazard pictograms	Not applicable
GHS Signal word	Not applicable
GHS Hazard statements	Not applicable
GHS Precautionary statements	Not applicable

Other hazards

Voretigene neparvovec is a recombinent adeno-associated viral vector derived from the naturally-occurring adeno-associated virus serotype 2 (AAV2), a member of the parvovirus family. The wild-type virus is naturally replication deficient, requiring co-infection with helper virus to replicate, and has not been associated with human disease.

AAV2 is a globally endemic virus with no known pathogenic potential, and genetic modifications made to generate voretigene neparvovec do not change the non-pathogenic nature. Voretigene neparvovec is administered via subretinal injection (between 2 tissues inside the eye) in a controlled surgical setting. Other routes of exposure were not studied in humans. Trace systemic exposure and shedding from patient tears was detected transiently after subretinal administration during clinical trials, but the likelihood of exposure to unintended recipients via tears is considered minimal. The pharmacy manual provides guidance and precautions for patients and caregivers to further limit the remote possibility of inadvertent environmental exposure.

The safety profile of voretigene neparvovec is generally consistent with complications of intraocular surgery, including vitrectomy and subretinal injection, although adverse reactions (incidence ≥ 5%) reported in subjects may have been related to voretigene neparvovec, concomitant use of corticosteroids, or a combination of these procedures and products. The established safety profile of voretigene neparvovec is published in the US Prescribing Information.

Note

The specified product does not meet criteria for classification 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). Nevertheless, it should be handled with caution as it contains a viral vector, and biohazards are specifically excluded from these regulations.

The product is considered Risk Group 1 (RG1) per the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules. A site specific risk assessment should be performed by competent EHS personnel to establish appropriate containment in line with local, state, and federal regulations.

SECTION 3: Composition/information on ingredients

Ingredient	CAS number	EINECS/ELINCS#	Amount	GHS classification
AAV2-hRPE65v2	1646819-03-5	N/A	Confidential	Not classified

Note The ingredient(s) listed above is not classified, but is listed because it may represent a biological hazard. The remaining ingredients are nonhazardous or present below reportable limits.

SECTION 4: First-aid measures

Description of first aid measures

Immediate medical attention and special treatment, if necessary No

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. See a physician to monitor for signs of infection.

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. See a physician to monitor for signs of infection.

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. See a physician to monitor for signs of infection.

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.

Unsuitable extinguishing media None known.

Specific hazards arising from the chemical Not tested. May emit carbon monoxide and carbon dioxide.

Fire hazard Not tested. As product is an aqueous solution, it is not expected to be flammable.

Explosion hazard Not tested. As product is an aqueous solution, it is not expected to be explosive.

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 vapors/mist/spray.

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 sample is spilled, avoid aerosolization.. Spills should be treated as biohazardous/ infectious material. Wear appropriate personal protective equipment including gloves, lab coat, and safety glasses. Cover the spill with absorbent material and apply disinfectant for appropriate contact time recomended by the manufacturer., Note: ethanol/isopropyl alcohol based disinfectants are not effectve.

Other information Dispose of all potentially contaminated materials as biohazardous waste according to local biosafety regulations and guidelines.

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

SECTION 7: Handling and storage

Precautions for safe handling Voretigene neparvovec requires at a minimum Biosafety Level 1 (BSL-1) work practices, containment and controls, and laboratory/facilities. Additional recommendations for appropriate handling are outlined in Section 8 (i.e, use of engineering controls and/or other personal protective equipment if needed). Avoid breathing vapor/mist/spray. Wash hands thoroughly after handling.

Conditions for safe storage, including any incompatibilities

Storage conditions Keep container tightly closed. Keep upright. Keep away from moisture, heat, direct light. Do not shake.

Storage temperature $\leq$ -65 °C

Specific end use(s) Pharmaceuticals

SECTION 8: Exposure controls/personal protection

Note Voretigene neparvovec is considered Risk Group 1 (RG1) per the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

Control parameters/Occupational Exposure Limits

Name	Issuer	Value
AAV2-hRPE65v2	No data available	No data available

Appropriate engineering controls Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use properly maintained Class II Biosafety Cabinet (BSC), engineered local exhaust ventilation (LEV), and/or enclosure for procedures where aerosolization may occur such as opened transfers, pumping, and spraying. Solutions can be handled outside a containment system or without LEV during procedures with no potential for aerosolization. All containers for solutions and slurries must be covered while being transferred.

Respiratory protection Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls.

Hand protection Wear nitrile or other impervious gloves if skin contact is possible.

Eye 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.

Skin and body protection Wear protective clothing appropriate to the task and safety glasses with side shields. Ensure gloves are protective against solvents in use. Protective garments (coveralls, disposable coveralls, lab coats) are not to be worn in common areas (e.g., cafeterias) or out-of-doors.

Other protective measures Use safe sharp precautions. Wash hands after all work and immediately in the event of contact with the substance, especially before eating, drinking, or smoking.

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	Liquid
Appearance	Clear liquid
Formula	Mixture - Not applicable
Molecular mass	Mixture - Not applicable
Colour	Clear
Odour	Not tested
Odour threshold	Not tested
pH	7.3
Melting point	Not tested
Freezing point	Not tested
Boiling point	Not tested
Flash point	Not tested
Relative evaporation rate (butylacetate=1)	Not tested
Flammability (solid, gas)	Not tested
Vapour pressure	Not tested
Relative vapour density at 20°C	Not tested
Relative density	Not tested
Solubility	Not tested
Log Pow	Not tested
Auto-ignition temperature	Not tested
Decomposition temperature	Not tested
Viscosity, kinematic	Not tested
Viscosity, dynamic	Not tested
Explosive limits	Not tested
Explosive properties	Not tested
Oxidising properties	Not tested

SECTION 10: Stability and reactivity

Reactivity	The product is non-reactive under normal conditions of use, storage and transport.
Chemical stability	Chemically stable; pharmacological stability not guaranteed beyond expiration date imprinted on package.
Possibility of hazardous reactions	No dangerous reactions known under normal conditions of use.
Conditions to avoid	(See section 7: Handling and Storage).
Incompatible materials	No data available
Hazardous decomposition products	Under normal conditions of storage and use, hazardous decomposition products should not be produced.

SECTION 11: Toxicological information

Acute toxicity

Component	Type	Dose
AAV2-hRPE65v2	No data available	No data available

Additional information	Not tested
Serious eye damage/irritation	Not tested
Skin corrosion/irritation	Not tested
Sensitisation	Not tested
STOT-single exposure	Not tested
STOT-repeated exposure	Not tested
Reproductive toxicity	Not tested
Developmental toxicity	Not tested
Genotoxicity	Not tested

Carcinogenicity	Not tested
Aspiration hazard	Not tested
Potential adverse human health effects and symptoms	See "Section 2 - Other Hazards".

SECTION 12: Ecological information

Toxicity

Component	Type	Concentration
AAV2-hRPE65v2	Not tested	Not tested

Persistence and degradability	Not tested
Bioaccumulative potential	Not tested
Mobility in soil	Not tested
Results of PBT assessment	Not tested
Other adverse effects	Not tested
Note	The environmental characteristics of the specified product have not been fully investigated, but it is not known to be associated with any environmental effects. Releases to the environment should be avoided.

SECTION 13: Disposal considerations

Waste treatment methods	Dispose of all potentially contaminated materials as biohazardous waste according to local biosafety regulations and guidelines.

SECTION 14: Transport information

Transport	Transport: Based on the available data, this specified product is not regulated as a hazardous material/dangerous good under US DOT. For international and/or air transport, this material is regulated by the IATA Dangerous Goods Regulations. IATA specification 3.9.2.5.1 states genetically modified micro-organisms (GMMOs) and genetically modified organisms (GMOs) are micro-organisms and organisms in which genetic material has been purposely altered through genetic engineering in a way that does not occur naturally. These materials must be assigned the proper shipping name and UN number and packaged according to Packing Instruction (PI) 959 for GMO/GMMOs.
UN number	UN 3245
UN proper shipping name	Genetically modified micro-organism (GMMO)
Transport hazard class(es) (DOT)	None assigned.
Packing group	None assigned.
Marine pollutant	Based on the available data, this specified product 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	Pharmaceuticals are exempt from TSCA.
SARA Section 313 - Emission Reporting	This substance or specified product 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	

SECTION 16: Other information

Full text of H phrases and GHS classification	Not applicable
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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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.