SAFETY DATA SHEET

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

Contact information

General

Celgene Corporation
86 Morris Avenue, Summit, NJ 07901
Main: +1 (908) 673-9000
E-mail: MSDScoordinator@Celgene.com

Emergency telephone number

Chemtrec *(24-hour availability)*:
+1 (800) 424-9300 (USA and Canada)
+1 (703) 527-3887 (International; collect calls accepted)

Product identifier Luspatercept lyophilized cake DP

Synonyms ACE-536

Trade names REBLOZYL®

Chemical family Mixture

Relevant identified uses of the substance or mixture and uses advised against Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product packaged in final form for patient use; indicated to treat anemia in adult patients with β-thalassemia..

Note The physical, chemical, toxicological and ecological properties of this product/ mixture and/or its ingredients have not been fully characterized. This SDS will be revisited as more data become available.

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.** Consult prescribing/packaging information. **The classification and labeling listed below is for bulk drug product.**

Globally Harmonized System [GHS] Specific Target Organ Toxicity (repeated exposure) - Category 1. Toxic to Reproduction - Category 1B.

SECTION 2 - HAZARDS IDENTIFICATION …continued

Label elements

GHS hazard pictogram

GHS signal word Danger

GHS hazard statements H372 - Causes damage to liver, kidneys, adrenals, and hematopoietic system through prolonged or repeated exposure. H360D - May damage the unborn child.

GHS precautionary statements P201 - Obtain special instructions before use. P202 - Do not handle until all safety precautions have been read and understood. P260 - Do not breathe dust/mist/vapors/spray. 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.

Other hazards Luspatercept is a human recombinant fusion protein. It was administered by subcutaneous (SC) injection to healthy volunteers and patients in clinical trials. Common effects in healthy volunteers included injection site reactions (hemorrhage or color change), dry skin, muscle spasms, muscle pain, itchiness, and rash. In patients, bone/musculoskeletal pain, headache, weakness, fever, cold- or flu-like symptoms, fatigue, hypertension, and gastrointestinal upset frequently occurred.

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 #	EINECS/ ELINCS#	Amount	GHS Classification
Luspatercept	1373715-00-4	N/A	30-50%	STOTR1: H372; RT1B: H360D
Trisodium citrate dihydrate	6132-04-3	612-118-5	1-5%	SI2: H315; EI2: H319; STOT-S3: H335
Sucrose	57-50-1	200-334-9	50-60%	Not classified

Note The ingredients listed above are considered hazardous or are the active ingredient. The remaining components are non-hazardous and/or present at amounts below reportable limits. Sucrose is included because it has OELs. See Section 16 for full text of 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	No specific first aid measures required. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. If signs/symptoms occur or if concerned, get medical attention.
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 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 carbon monoxide, carbon dioxide, oxides of nitrogen.
Flammability/ Explosivity	No explosivity or flammability data identified. High concentrations of finely divided airborne organic particles can potentially explode if ignited.
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 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. Do not breathe dust.
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 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	Follow recommendations for handling potent pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing dust. Wash thoroughly after handling. Avoid exposure to light.
Conditions for safe storage including any incompatibilities	Store refrigerated at 2-8 °C away from incompatible materials. Avoid extreme temperatures.
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Luspatercept	Celgene	TWA-8 HR	100 µg/m³
Trisodium citrate dihydrate	--	--	--
Sucrose	ACGIH	TLV-TWA	10 mg/m3
	Belgium	OEL TWA	10 mg/m3 (8-hr TWA)
	Bulgaria	OEL-TWA	10 mg/m3 (respirable dust)
	Canada	OEL-TWA	10 mg/m3
	Canada - Northwest Territories, Nunavut	OEL-TWA	5 mg/m3 (respirable dust)

Control Parameters/ Occupational Exposure Limit Values

…continued

Compound	Issuer	Type	OEL
	Canada - British Columbia	OEL-TWA	3 mg/m3 (respirable dust)
	Canada - Saskatchewan, Yukon	OEL - STEL	20 mg/m3
	Estonia	OEL-TWA	10 mg/m3
	France	OEL-TWA (VME)	10 mg/m3
	Ireland	OEL-TWA	10 mg/m3
	Ireland	OEL-STEL	20 mg/m3
	Latvia	OEL-TWA (AER)	5 mg/m3
	Lithuania	OEL-TWA (IPRV)	10 mg/m3
	NIOSH	REL-TWA	5 mg/m3 (respirable dust); 10 mg/m3 (total dust)
	Portugal	OEL-TWA	10 mg/m3
	Slovakia	OEL-TWA	6 mg/m3 (total aerosol)
	Spain	OEL-TWA (VLA-ED)	10 mg/m3
	United Kingdom	WEL-TWA	10 mg/m3
	United Kingdom	WEL-STEL	20 mg/m3

Exposure/Engineering controls

None required for normal handling of packaged product. If product is released, 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. Use local exhaust and/or enclosure at dust-generating points. Use specifically designed and engineered local exhaust ventilation (LEV) and/or enclosure at dust-generating points and for high dust-generating operations. Limited open handling allowable for low dust-generating operations. Emphasis is placed on closed material transfer through direct connections, dust control and containment using LEV, certified downflow booths, glove bags, process containment via intermediate bulk containers (IBCs) with split butterfly valves (SBVs) and/or isolator technology.

Respiratory protection

None required for normal handling of packaged product. If product is released, or if handling bulk formulation: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. At a minimum, a tight-fitting full-face respirator with HEPA filters is required when performing dust or aerosol generating operations. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required for spill cleanup.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Hand protection	None required for the normal handling of packaged product. 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 disposable coveralls appropriate to the task, booties, 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. Employees must be trained in proper gowning and degowning practices.
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	Solid (lyophilized cake)
Color	No information identified.
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	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

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 formula	Not applicable (Mixture)
Molecular weight	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable when stored as recommended.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	None expected under normal conditions.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note No data for this product/mixture were identified. The following data describe the active ingredient.

Information on toxicological effects

Route of entry May be absorbed by inhalation. Systemic absorption following ingestion or through skin is not likely.

Acute toxicity

Compound	Type	Route	Species	Dose
Luspatercept	--	--	--	--
Trisodium citrate dihydrate	--	--	--	--
Sucrose	LD_{50}	Oral	Rat	29,700 mg/kg

Irritation/Corrosion No data available.

Sensitization No data available.

STOT-single exposure No data available.

STOT-repeated exposure/Repeat-dose toxicity Findings in SC rat studies included decreased heart, lung, and prostate weights and damage to the adrenal gland, liver, glandular stomach, and kidneys. The effects were dose dependent, and were noted at ≥1 mg/kg administered every two weeks (0.07 mg/kg/day) in a 13-week study. Kidney damage was also noted in a 6-month monkey study at doses ≥1 mg/kg administered every 2 weeks (0.07 mg/kg/day), along with damage to the choroid plexus, a structure in the brain that produces cerebrospinal fluid. The effects at the lowest dose (0.3 mg/kg; 0.04 mg/kg/day) were limited to anticipated effects on red blood cells.

Reproductive toxicity Female rats intermittently administered 15 mg/kg luspatercept SC during mating and early gestation (a total of 3 doses) had significant reductions in the number of corpora lutea and implantations, which were reversible in a subsequent study after a 14-week recovery period. Male rats treated intermittently before and during mating (a total of 4 doses) had no adverse effects. The reported paternal and maternal NOAELs were 15 and 3 mg/kg/dose, respectively.

Developmental toxicity Luspatercept was administered SC to pregnant rats and rabbits twice, on gestation days 3 and 10 or 4 and 11, respectively. In rats, decreased uterine weight was reported at all doses, ≥5 mg/kg, while reduced fetal body weights and skeletal variations were reported at 15 mg/kg, and maternal toxicity and fetal deaths occurred at 30 mg/kg. A decrease in viable fetuses was also observed in female rats given 3 doses of 15 mg/kg throughout mating/early gestation. In rabbits, reduced litter sizes and increased resorptions were only reported at doses that also caused maternal toxicity, which were ≥20 mg/kg. The NOAEL for both species was 5 mg/kg.

In a pre- and postnatal development study, pregnant rats were administered luspatercept at SC doses of 3, 10, or 30 mg/kg once every 2 weeks during organogenesis and through weaning. At all dose levels tested lower pup body weights and adverse kidney findings were observed. A NOAEL was not identified.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Genotoxicity No data available.

Carcinogenicity No definitive studies were identified. Hematological malignancies were reported in a repeat-dose toxicity study with juvenile at a SC dose of 10 mg/kg, once every 2 weeks. The relevance of this finding to humans is unclear. None of the components of this 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
Luspatercept	--	--	--
Trisodium citrate dihydrate	--	--	--
Sucrose	--	--	--

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 No data available.

Note The environmental characteristics of this product/mixture have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods Dispose of wastes by appropriately permitted chemical waste incinerator in accordance to prescribed federal, state, and local guidelines. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, *e.g.*, appropriately permitted municipal or onsite 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 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.
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 H phrases and GHS classifications	STOT-R1 - Specific Target Organ Toxicity Following Repeat Exposure Category 1. H372 - Causes damage to liver, kidneys, adrenals, and hematopoietic system system through prolonged or repeated exposure. RT1B - Reproductive toxicity Category 1B. H360D - May damage the unborn child. SI2 - Skin irritant Category 2. H315 - Causes skin irritation. EI2 - Eye irritant Category 2. H319 - Causes serious eye irritation. STOT-S3 - Specific Target Organ Toxicity Following Single Exposure Category 3. H335 - May cause respiratory irritation.
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 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	4 February 2020
Revisions	Updated marketing status. Updated OEL and handling recommendations in Section 8. Updated data in Section 11.
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

Disclaimer …continued

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.