SAFETY DATA SHEET

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

Contact information

General

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Product identifier

ZEPOSIA™ (Ozanimod) Capsules

Synonyms

For ozanimod hydrochloride: RPC1063; 5-(3-{(1S)-1-[(2-hydroxyethyl)amino]-2,3-dihydro-1*H*-inden-4-yl}-1,2,4-oxadiazol-5-yl)-2-[(propan-2-yl)oxy]benzonitrile, monohydrochloride.

Trade names

ZEPOSIA™

Chemical family

Mixture - contains a bi-aryl oxadiazole derivative

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; indicated for the treatment of relapsing multiple sclerosis (RMS), as well as for moderate-to-severe inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease.

Note

This SDS is written to address potential worker health and safety issues associated with the handling of the formulated drug product.

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 labelling listed below is for bulk drug product.**

Globally Harmonized System [GHS]

Reproductive Toxicity - Category 1B. Specific Target Organ Toxicity (repeated exposure) - Category 1.

SECTION 2 - HAZARDS IDENTIFICATION …continued

Label elements

GHS hazard pictogram

GHS signal word

Danger

GHS hazard statements

H360D - May damage the unborn child. H372 - Causes damage to bone marrow and lymphoid tissue through prolonged or repeated exposure.

GHS precautionary statements

P201 - Obtain special instructions before use. P260 - Do not breathe dust. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. 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

Ozamimod is a potent, immunomodulating drug. Adverse effects reported in clinical trials were mild-to-moderate in severity (including headache, upper respiratory and urinary tract infections, back pain, and minor heart rate/blood pressure changes) and their incidence rate was similar to placebo. Increased incidence of local herpes infections were also reported.

Note

This product/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
Cellulose	9004-34-6	232-674-9	96-98 %	Not classified
Ozanimod	1306760-87-1	N/A	0.1-1.0 %	ATO4: H302; RT1B: H360D; STOT-R1: H372

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 GHS classifications. Cellulose (in microcrystalline form) is included because it has OELs and is present at or above 1%. Amounts are listed as ranges; the exact percentage of composition is withheld as a trade secret.

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 carbon monoxide, carbon dioxide, oxides of nitrogen, and other magnesium- and/or silica-containing compounds.
Flammability/ Explosivity	No explosivity or flammability data identified. High concentrations of finely divided airborne 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. 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	If capsules are broken or crushed, 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	If capsules 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. Avoid breathing dust.
Conditions for safe storage including any incompatibilities	Store at room temperature (25°C; 77°F) away from incompatible materials; excursions permitted to 15-30°C. Do not refrigerate or freeze.
Specific end use(s)	Pharmaceutical.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Cellulose	ACGIH, Australia, Belgium, Estonia, France, Portugal, Romania, Singapore, Spain	TWA-8 HR	10 mg/m³

Control Parameters/ Occupational Exposure Limit Values

…continued

Compound	Issuer	Type	OEL
	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)
Ozanimod	Celgene	8-hour TWA	2 µg/m³

Exposure/Engineering controls

None required for normal handling of packaged product. If handling bulk capsules or capsules are crushed or broken: Open handling should not be performed when handling potent substances or substances of unknown toxicity. Control exposures to below the OEL of the active ingredient. Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

Respiratory protection

None required for normal handling of packaged product. If handling bulk capsules or capsules are crushed or broken: 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. Wear nitrile or other impervious gloves if skin contact with capsules is possible. Double gloves may be considered.

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.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

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	Opaque hard gelatin capsules imprinted with black ink
Color	(0.25 mg) Light gray body and light gray cap (0.5 mg) Light gray body and orange cap (1.0 mg) Orange body and orange cap
Odor	Odorless
Odor threshold	No information identified.
pH	No information identified.
Melting point/ freezing point	221°C to 227°C (ozanimod)
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.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Water solubility	For ozanimod: Poorly hydroscopic; Mostly soluble in acidic solutions (pH <5).
Solvent solubility	For ozanimod: Mostly soluble in methanol, ethanol, and polyethylene glycol (PEG400); Poorly soluble in acetonitrile and isopropanol.
Partition coefficient (*n-octanol/water*)	logP = 3.28 (ozanimod)
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	Chemically stable; pharmacological stability not guaranteed beyond expiration date imprinted on package.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	Avoid extreme temperatures.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note	No data for this product/mixture were identified. 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
Cellulose	LC_{50}	Inhalation	Rat	>5800 mg/m³/4h
	LD_{50}	Oral	Rat	>5000 mg/kg
	LD_{50}	Dermal	Rabbit	>2000 mg/kg
Ozanimod	Minimum Lethal Dose (MLD)	Oral (presumed)	Rat	≥200 mg/kg
	MLD	Oral (presumed)	Rabbit	≥50 mg/kg
	MLD	Oral (presumed)	Monkey	≥45 mg/kg
	MLD	Oral (presumed)	Dog	≥1.5 mg/kg

Irritation/Corrosion No studies identified.

Sensitization No studies identified.

STOT-single exposure No studies identified.

STOT-repeated exposure/Repeat-dose toxicity Repeated oral dose toxicity studies were conducted in mice for up to 28 days, and in rats and monkeys for up to 6 and 9 months, respectively. Dose-dependent and reversible decreases in white blood cell count (primarily lymphocytes), lymphoid depletion of the spleen with an associated decrease of spleen weight, and loss of corticomedullary differentiation in the thymus were noted in all three species at doses as low as 0.4, 0.2, and 0.1 mg/kg/day, respectively. An increase in myeloid elements in the bone marrow of monkeys was also noted.

Target organs of toxicity included lung (e.g., lung weight increase and histiocytosis in mice, rats, and monkeys), kidneys (e.g., anisocytosis and anisokaryosis of the proximal tubule in rats and monkeys), and small intestine (histiocytosis), adrenal gland (hypertrophy), and liver (hypertrophy and necrosis) only in monkey. These effects were fully or partially reversible in all species. The NOAELs in mice, rats, and monkeys, were reported as 0.4, 0.2, and 0.1 mg/kg/day, respectively.

Reproductive toxicity No adverse effects on reproductive performance and fertility were noted in rats treated orally with doses up to 30 mg/kg/day ozanimod.

Developmental toxicity Ozanimod was both embryotoxic and teratogenic in rats and rabbits at oral doses of 5 and 0.6 mg/kg/day, respectively. Adverse effects included edema, delayed ossification, and blood vessel abnormalities. The rat and rabbit NOAELs were 1 and 0.2 mg/kg/day respectively. In pre- and post-natal studies in rats, there were no adverse effects in the dams and the offspring at the highest administered oral dose (2 mg/kg/day), which was deemed to be a NOAEL.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Genotoxicity

Ozanimod was negative for genotoxicity in the Ames bacterial mutagenesis assay, an *in vitro* mouse lymphoma TK+/- test, and an *in vivo* rat bone marrow micronucleus study.

Carcinogenicity

In an oral two-year carcinogenicity rat study, ozanimod (≤2 mg/kg/day) did not increase tumor incidence. In an oral 26-week carcinogenicity study in transgenic mice, an increase in the incidence of hemangiosarcoma/hemangioma was noted in male and female mice at ≥8 and ≥25 mg/kg/day. However, as spontaneous incidence of these types of tumors is high in mice, the the relevance of this finding to human health is unclear.

Aspiration hazard

No data available.

Human health data

See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Cellulose	--	--	--
Ozanimod	--	--	--

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

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 bone marrow and lymphoid tissue through prolonged or repeated exposure. RT1B - Reproductive toxicity Category 1B. H360D - May damage the unborn child. ATO4 - Acute Toxicity (Oral) Category 4. H302 - Harmful if swallowed.

SECTION 16 - OTHER INFORMATION …continued

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
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