SAFETY DATA SHEET

SDS Revision 0 (original)
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Nurtec™ ODT (rimegepant), 75 mg Safety Data Sheet

SECTION 1: PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME: **Nurtec™ ODT**

SYNONYMS: Rimegepant; (5S,6S,9R)-5-Amino-6-(2,3-difluorophenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-yl 4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-1-piperidinecarboxylate hemisulfate sesquihydrate; previously BMS-927711-11 and BHV-3000

DESCRIPTION: Oral Disintegrating Tablet (ODT) 75 mg

MANUFACTURER: Biohaven Pharmaceuticals, Inc.

ADDRESS: 215 Church St., New Haven, CT 06510

Phone #: 1-203-404-0410

PRODUCT USE: Commercial Pharmaceutical Product for the treatment of migraines

EMERGENCY PHONE NUMBER: For treatment advice, seek guidance from an occupational health physician or other licensed health-care provider familiar with workplace chemical exposures. In the United States, the national poison control center phone number is 1-800-222-1222.

SECTION 2: HAZARDS IDENTIFICATION

Classification of the substance or mixture
GHS Classification in accordance with 29 CFR 1910 (OSHA HCS)

Toxic To Reproduction - Developmental Toxicity - Category 2
Specific Target Organ Systemic Toxicity (Single Exposure) - Category 3
Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 2
Substance not fully tested.

GHS Label elements, including precautionary statements

Pictogram:

Signal word: Warning

Hazard statement(s)
H335: May cause respiratory irritation.
H361; Suspected of damagning the unborn child.
H373: May cause damage to organs through prolonged or repeated exposure.

Precautionary statement(s)
P201: Obtain special instructions before use.
P202: Do not handle until all safety precautions have been read and understood.
P260: Do not breathe dust.
P271: Use only outdoors or in a well-ventilated area.
P281: Use personal protective equipment as required.

Hazards not otherwise classified (HNOC) or not covered by GHS
None

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

Oral Disintegrating Tablet (ODT) 75 mg

Component	Classification	Conc. %
BHV-3000 (hemisulfate, sesquihydrate) MW (salt form): 610.63 MW (free base): 534.56 CAS-No. : 1374024-48-2	Toxic To Reproduction – Developmental Toxicity - Category 2 Specific Target Organ Systemic Toxicity (Single Exposure) - Category 3 Specific Target Organ Systemic Toxicity (Repeated Exposure) – Category 2 Xn: Harmful R48: Danger of serious damage to health by prolonged exposure. R63: Possible risk of harm to the unborn child. C-snft: Substance not fully tested. H361; Suspected of damagning the unborn child. H373: May cause damage to organs through prolonged or repeated exposure.	74.78
Gelatin (Fish HMW) (USP/EP/JP) CAS-No. : 9000-70-8 EC-No. : 232-554-6	No classification reqired	5-20%
Mannitol (USP/EP/JP) CAS-No. : 69-65-8 EC-No. : 207-711-8	No classification reqired	5-15%
Other Ingredients: Non-Hazardous Ingredients CAS-No. : Proprietary EC-No. : Proprietary	No data available	< 5%

SECTION 4: FIRST AID MEASURES

DESCRIPTION OF FIRST AID MEASURES

GENERAL ADVICE: Consult a physician. Show this safety data sheet to the doctor in attendance. Move out of dangerous area. Material not fully tested. Refer to Section 11.

EYES: Rinse immediately with plenty of water for at least 15 minutes. Keep eye wide open while rinsing. If exposed or concerned: Get medical attention/advice.

SKIN: Take off contaminated clothing and shoes immediately. Wash immediately with plenty of water for at least 15 minutes. Discard contaminated clothing or wash before re-use. If exposed or concerned: Get medical attention/advice

INGESTION: Do NOT induce vomiting. Never give anything by mouth to an unconscious person. If exposed or concerned: Get medical attention/advice.

MOST IMPORTANT SYMPTOMS/EFFECTS, ACUTE AND DELAYED: The most important known symptoms and effects are described in the labelling (see section 2) and/or in section 1

INDICATION OF IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT NEEDED: The need for a pre-placement physical examination and history for employees with potential exposure to this compound is to be evaluated by a physician that is thoroughly knowledgeable about both the toxicity of this compound and the extent of work place exposure. Baseline testing would include: a complete blood count with differential, a blood test for liver function. Based on opportunity for exposure and duration of exposure a periodic follow-up examination may be considered.

Employees who are pregnant, are breast-feeding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational health physician monitoring worker's health.

SECTION 5: FIRE-FIGHTING MEASURES

EXTINGUISHING MEDIA: Suitable extinguishing media: Dry chemical, Water spray, Foam
Unsuitable extinguishing media: Do NOT use water jet.

SPECIFIC HAZARDS ARISING FROM CHEMICAL: no data available

SPECIAL FIRE FIGHTING PROCEDURES:
Protective equipment: Use personal protective equipment. In the event of fire, wear self- contained breathing apparatus.
Hazardous Combustion Products: carbon oxides (COx), nitrogen oxides (NOx), hydrogen fluoride in combination with fluoride. Hydrogen halide gases can react with metals to form potentially explosive hydrogen/air mixtures. In the event of fire and/or explosion do not breathe fumes.

FURTHER INFORMATION: Decontaminate protective clothing and equipment before reuse.

SECTION 6: ACCIDENTAL RELEASE MEASURES

ACCIDENTAL RELEASE MEASURES: Wear respirator, chemical safety goggles, rubber boots, and heavy rubber gloves . Avoid raising dust. Use proper absorbent materials or a HEPA filtered vacuum for small spills. For large spills, appropriate emergency response personnel should be notified. Ventillate area well. Keep personnel away from the clean-up area.

PERSONAL PRECAUTIONS, PROTECTIVE EQUIPMENT AND EMERGENCY PROCEDURES:
Refer to protective measures listed in sections 7 and 8. Use personal protective equipment.
Examples include tightly fitting safety goggles, disposable lab coat of low permeability with cuffs, double gloves and shoe covers. Wear respiratory protection. Depending on the nature of the spill (quantity and extent of spill) additional protective clothing and equipment such as a self-contained breathing apparatus may be needed.

ENVIRONMENTAL PRECAUTIONS: Prevent release to drains and waterways. Prevent release to the environment.

METHODS AND MATERIALS FOR CONTAINMENT AND CLEANING UP:
Wet down any dust to prevent generation of aerosols, if appropriate. Cover with suitable material.
Spill prevention procedures and a spill response procedure should be implemented.
Contain and collect spillage and place in container for disposal according to local regulations (see Section 13).
Clean spill area with a deactivating solution (if available) followed by detergent and water after spill pick-up.
Handle waste materials, including gloves, protective clothing, contaminated spill cleanup material, etc., as appropriate for chemically and pharmacologically similar materials.

SECTION 7: HANDLING AND STORAGE

PRECAUTIONS FOR SAFE HANDLING: Highly potent material. Avoid formation of dust and aerosols. Avoid exposure - obtain special instructions before use. When handling broken or crushed tablets or capsules, ensure worker exposure is below the recommended exposure limit. Keep away from heat and sources of ignition.
Prevent release to drains and waterways.
For precautions see section 2.

CONDITIONS FOR SAFE STORAGE, INCLUDING ANY INCOMPATIBILITIES:

Store at room temperature. Protect against light. Keep away from heat, sparks and flames.

Store locked up. Store in well-ventilated place. Keep container tightly closed.
Store in the original primary packaging as provided. Keep container tightly closed.

SPECIFIC END USE(S): Apart from the uses mentioned in section 1 no other specific uses are stipulated

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

CONTROL PARAMETERS:

BHV-3000: OEL (Biohaven Pharmaceuticals): 20 µg/m^3

There are no other known established exposure control limits

ENGINEERING CONTROLS: FOR MANUFACTURING PROCESSES (BULK): Use process enclosures, containment technology, or other engineering controls to keep airborne levels below recommended exposure limit. When handling quantities up to 3 milligrams, a standard laboratory with general laboratory dilution ventilation (e.g. 6-12 air changes per hour) is appropriate. When handling quantities up to 1 kilogram, work in either a standard laboratory (<500 g) or designated laboratory (500 g to <1 kg) using a fume hood, biological safety cabinet(Class II, Type A2 with thimble connection, B1, or B2)or approved vented enclosure. HEPA filtered exhaust preferred for fume hoods containing particularly "dusty" operations. Quantities exceeding 1 kilogram should be handled in a designated laboratory or containment facility using appropriate containment technology. A laminar flow/powder containment booth or appropriate isolation technology should be considered for handling more than 1 kilogram of active compound. HEPA filtered exhaust preferred. For manufacturing and pilot plant operations, barrier/containment technology and direct coupling (totally enclosed processes that create a barrier between the equipment and the room) with use of double or split butterfly valves, hybrid unidirectional airflow/local exhaust ventilation solutions (e.g. powder containment booth) should be used. Glove bags, isolator/glove box systems are optional. HEPA filtration of exhaust from dry product handling areas is required.

FOR CLINICAL SETTING USE (DRUG PRODUCT): When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed. When handling broken or crushed tablets or capsules, ensure worker exposure is below the recommended exposure limit. If significant dust is generated, use process enclosures, containment technology, or other engineering controls to keep airborne levels below recommended exposure limit.

PERSONAL PROTECTION: This formulation contains an active pharmaceutical ingredient (API) with the guideline limit noted above. To keep the API below the recommended guideline, the material as supplied should be controlled during handling to limit total airborne aerosol exposure to: 2 µg/m^3.

EYE/FACE PROTECTION: Safety glasses with side-shields are recommended (EN 166). Face shields or chemical safety goggles (EN 166) may be required if splash potential exists or if corrosive materials are present. Note: Choice of eye protection may be influenced by the type of respirator which is selected.

SKIN PROTECTION: Wear gloves at all times when handling containers, including when unpacking, inspecting or transporting within a facility. Impervious gloves are recommended. (EN 420, EN 374). Double gloving for all manufacturing personnel potentially in direct contact with the compound should be considered. If material is handled in solution, the solvent should also be considered when selecting protective clothing material. Wash hands and face before breaks and immediately after handling the product.

BODY PROTECTION: Wear a laboratory coat (EN 340) when handling quantities up to 500 grams. For quantities up to 1 kilogram, wear disposable laboratory coat (EN 340) or coverall of low permeability (EN1149-1) . For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability (EN 1149-1) and disposable shoe covers. FOR CLINICAL SETTING USE (DRUG PRODUCT): Follow good chemical hygiene practices when using clinical or consumer presentations. It is recommended that a laboratory coat be worn when handling product.

RESPIRATORY PROTECTION: Use and selection of respiratory protection is based upon engineering controls in use and potential for aerosol generation. When engineering controls are not sufficient control exposure, wear an approved respirator with NIOSH Class 100 or high efficiency particulate (HEPA) filters or cartridges (EN 140/EN 136) when exposures are up to 10 times the exposure control guideline. Wear a loose-fitting (Tyvek or helmet type) HEPA powered-air purifying respirator (PAPR) (EN 12941) when exposures are 10-25 times the exposure control guideline. Wear a full facepiece negative pressure respirator with Class 100 or HEPA filters (EN 136) when exposures are 25-50 times the exposure control guideline. Wear a tight- fitting, full facepiece HEPA PAPR (EN 12942) when exposures are 50-100 times the exposure control guideline. Wear a hood-shroud HEPA PAPR (EN 12941) or full facepiece supplied air respirator (EN 139) operated in a pressure demand or other positive pressure mode when exposures are 100-1000 times the exposure control guideline.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

a) Appearance Form:	ODT : White to off-white, circular, freeze-dried units ablet
b) Odor	No data available
c) Odor Threshold	No data available
d) pH	No data available
e) Melting point/freezing point	No data available
f) Initial boiling point & boiling range	No data available
g) Flash point	No data available
h) Evaporation rate	No data available
i) Flammability (solid, gas)	No data available
j) Upper/lower flammability or explosive limits	No data available
k) Vapour pressure	No data available
l) Vapour density	No data available
m) Relative density	No data available
n) Water solubility	No data available
o) Partition coefficient: n-octanol/water	No data available
p) Auto-ignition temperature	No data available
q) Decomposition temperature	No data available
r) Viscosity No data available	No data available
s) Explosive properties	No data available
t) Oxidizing properties	No data available

SECTION 10: STABILITY AND REACTIVITY

REACTIVITY : no data available

CHEMICAL STABILITY: No data available

POSSIBILITY OF HAZARDOUS REACTIONS: None known

CONDITIONS TO AVOID: No data available

INCOMPATIBLE MATERIALS: No data available

HAZARDOUS DECOMPOSITION PRODUCTS: Hazardous decomposition products formed under fire conditions: carbon oxides (COx), nitrogen oxides (NOx), hydrogen fluoride in combination with fluoride.

Sensitivity to static discharge/dust explosion

SECTION 11: TOXICOLOGICAL INFORMATION

Possible Routes of Exposure: Inhalation, Ingestion, Skin, Eye

ACUTE TOXICITY: Nurtec™ ODT

LD_{50} (rat, males and females): > 300 mg/kg No mortality occurred.
LD_{50} (monkey, males and females): > 300 mg/kg low exposure effects include (<= 300 mg/kg): tremors, behavioral changes.
Acute Telemetry study in Monkey: No significant cardiovascular or hemodynamic effects noted.

REPEATED DOSE TOXICITY Nurtec™ ODT
1 week – 1 month oral (daily) rat, monkey study with recovery period (2 weeks) (males and females): NOAEL = 20 mg/kg; Low dose effects include (≤ 100 mg/kg): increased prothrombin time, abdominal distention, vomiting, decreased food consumption, changes in red blood cell parameters, changes in white blood cell parameters, changes in white blood cell parameters, changes in clinical chemistry parameters, increased liver weight. High dose effects include: decreased body weight, changes in organ weights, mortality. Low dose microscopic effects include: liver, adrenal glands. High dose microscopic effects include: spleen, lymph nodes, thymus, lungs, muscle, stomach, pancreas.
There were no findings in the six (6) month rat study at doses up to 40 mg/kg/day or in the nine (9) month study at doses up to 50 mg/kg/day.
Human oral clinical trial(s) 14 days 1,500 mg. low exposure - acute effects include: nausea, vomiting, loss of appetite, constipation, dizziness, headache, rash, changes in clinical chemistry parameters

RESPIRATORY OR SKIN SENSITIZATION: Nurtec™ ODT
Negative for skin sensitization when tested at a concentration of 1%
Gelatin: Risk for hypersenstitivity in those with a fish allergy is not an issue at the level present. FDA's "Approaches to Establish Thresholds for Major Food Allergens and for Gluten in Food" reports that 0.5% of the US adult population has a fish allergy "However, in a recent double-blind placebo-controlled food challenge (DBPCFC) study, all 30 fish allergic subjects in the study showed no response to a cumulative dose of 3.61 g of fish gelatin (Hansen et al., 2004)."

GERM CELL MUTAGENICITY: Nurtec™ ODT

In vitro:	Ames reverse-mutation assay – negative
	In vitro cytogenicity study in mammalian cells – negative
In vivo:	3 days oral, micronucleus assay (rat) – negative

CARCINOGENICITY: This material did not show carcinogenic potential in animal studies. Not classifiable as to its carcinogenicity in humans.

IARC: No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

ACGIH: No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by ACGIH.

NTP: No component of this product are present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by NTP.

OSHA: No component of this product are present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by OSHA.

SECTION 11: TOXICOLOGICAL INFORMATION CONTINUED

REPRODUCTIVE & DEVELOPMENTAL TOXICITY

Nurtec™ ODT
Oral Study of Embryo-Fetal Development (rat)
(parent, females) NOAEL = 60 mg/kg
(embryo/fetus) NOAEL = 60 mg/kg
Fetal effects include: decreased body weight, changes in skeletal development.
Maternal effects include: decreased body weight, decreased food consumption, fecal changes, changes in red blood cell parameters, changes in clinical chemistry parameters, liver effects.
Oral study of embryo-fetal development (rabbit)
(parent, females) NOAEL = 25 mg/kg
(embryo/fetus) NOAEL = 50 mg/kg
Maternal effects include: decreased body weight, decreased food consumption, dehydration, fecal changes, hypoactivity, mortality. No effects were observed in the fetus/embryo. Developmental studies conclude that adverse effects on the fetus occur only at maternally toxic dose levels.
No effects on perinatal or postnal development

SPECIFIC TARGET ORGAN TOXICITY - SINGLE EXPOSURE: Blood, cardiovascular system, liver, lymphoid system

SPECIFIC TARGET ORGAN TOXICITY - REPEATED EXPOSURE: Blood, cardiovascular system, liver, lymphoid system

ASPIRATION HAZARD: no data available

ENVIRONMENTAL OVERVIEW: The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided.

ADDITIONAL INFORMATION
RTECS: Not available

PROLONGED OR REPEATED EXPSORUE MAY CAUSE:
Nurtec™ ODT
see repeat dose toxicity section.

OTHER INFORMATION: Not available
EIIMINATION HALF-LIFE: Nurtec™ ODT 11-18 hours
IN VITRO PHOTOTOXICITY: Nurtec™ ODT: negative

SECTION 12: ECOLOGICAL INFORMATION

This preparation has not been subjected to ecotoxicological testing as an entity. Release to the environment should be avoided

TOXICITY: no data available
PERSISTENCE AND DEGRADABILITY: no data available
BIOACCUMULATIVE POTENTIAL: no data available
MOBILITY IN SOIL: no data available
RESULTS OF PBT AND vPvB ASSESSMENT: PBT/vPvB assessment not available as chemical safety assessment not required/not conducted
OTHER ADVERSE EFFECTS: no data available

SECTION 13: DISPOSAL CONSIDERATIONS

WASTE DISPOSAL METHOD:
Disposal should be in accordance with applicable regional, national and local laws and regulations. Local regulations may be more stringent than regional or national requirements. This information presented only applies to the material as supplied. Disposal by incineration is recommended.

SECTION 14: TRANSPORT INFORMATION

DOT (US) / IMDG / IATA
Not dangerous goods

SECTION 15: REGULATORY INFORMATION

SARA 313 COMPONENTS:
This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

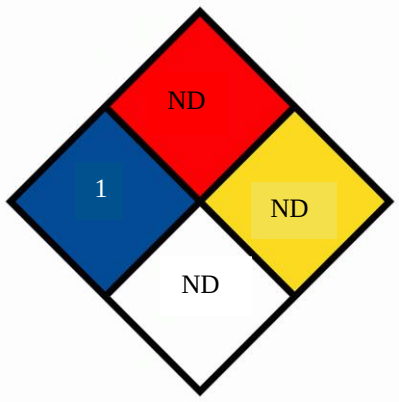
TSCA INVENTORY:
Not listed**.** Food, drug, and cosmetic products are exempt from TSCA.

DRUG PRODUCT CLASSIFICATION:
Medicinal products are exempt from classification and labeling requirements under EU Preparations Directive 1999/45/EC.

SECTION 16: OTHER INFORMATION

TEXT OF SYMBOLS, R-phrases, and H-codes mentioned in Section 3

C-snft	Caution - substance not yet fully tested.
H335	May cause respiratory irritation
H361d	Suspected of damaging the unborn child
H373	May cause damage to organs through prolonged or repeated exposure.
R37	Irritating to respiratory system.
R48	Danger of serious damage to health by prolonged exposure.
R63	Possible risk of harm to the unborn child.
Xi	Irritant
Xn	Harmful



HMIS Rating

Health hazard:	1
Chronic Health Hazard:	No data available
Flammability:	No data available
Physical Hazard:	See section 8

NFPA Rating

Health hazard:	1
Fire Hazard:	No data available
Reactivity Hazard:	No data available
Special :	No data available

Further information
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