1. Product and Company Identification

PRODUCT NAME: DOXERCALCIFEROL CAPSULES 0.5 mcg, 1 mcg, 2.5 mcg

Substance name: Doxercalciferol

Synonyms: 1α-hydroxyvitamin D2; 1α-OH-D2; 1α-hydroxyergocalciferol

Supplier:
Supplier:
Winthrop U.S.
A business of Sanofi U.S.
55 Corporate Drive
Bridgewater, NJ 08807

24-Hour Transport Emergency, US (Chemtrec):	**(800) 424-9300**
24-Hour Transport Emergency, outside US (Chemtrec):	**(703) 527-3887**
US Customer Service	**(800) 207-8049**
24-Hour Emergency, sanofi-aventis US:	**(908) 981-5550**

Product use: Pharmaceutical product.

2. Hazards Identification

2.1 Classification in accordance with 29 CFR 1910.1200

The finished product is not classified as a hazardous mixture. The concentration of the active ingredient doxercalciferol is 0.5, 1 or 2 micrograms per capsule.

The following classification for the pure drug substance doxercalciferol is provided here for information:

Classification:
Acute toxicity, Category 1
Specific target organ toxicity - repeated exposure, Category 1

2.2 Label elements in accordance with 29 CFR 1910.1200

Labeling of the finished drug product is not required according to OSHA 29 CFR 1910.1200. The following information is provided for the drug substance, doxercalciferol:

Signal Word: Danger

Hazard Statement(s): Fatal if swallowed. Causes damage to organs through prolonged or repeated exposure if swallowed.

Symbol(s): Skull and crossbones; Health Hazard.

Precautionary Statement(s):

- Prevention: Do not breathe dust. Wash hands thoroughly after handling. Do not eat, drink or smoke when using this product.
- Response: If swallowed: Immediately call a poison center. Rinse mouth. Get medical attention if you feel unwell.
- Storage: Store locked up.
- Disposal: Dispose of in accordance with applicable regional, national and local laws and regulations.

2.3 Hazards Not Otherwise Classified (HNOC)

Not classified.

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3. Composition/Information on Ingredients

Chemical Name:	**Common Name:**	**CAS #:**	**Percentage or concentration range**
(1α,3β,5Z,7E,22E)-9,10-secoergosta-5,7,10(19),22-tetraene-1,3-diol	Doxercalciferol	54573-75-0	0.5, 1 or 2 micrograms per capsule

Inactive Ingredients: Each capsule also contains fractionated triglyceride of coconut oil, ethanol, and butylated hydroxyanisole (BHA). The capsule shells contain gelatin, glycerin and titanium dioxide. In addition, the 0.5 mcg capsule shells contain yellow iron oxide and FD&C Red No. 40, the 1 mcg capsule shells contain FD&C Yellow No. 6, and the 2.5 mcg capsule shells contain yellow iron oxide.

4. First Aid Measures

4.1 First aid procedures

Eye contact: In case of contact with product, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lenses if worn. Get medical attention.

Skin contact: In case of contact with product, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention if irritation develops and persists.

Ingestion: If swallowed, call a poison center or physician immediately. Do NOT induce vomiting unless directed to do so by a physician. Never give anything by mouth to an unconscious person. Rinse mouth thoroughly with water.

Inhalation: If product is inhaled, remove to fresh air. If breathing is difficult, trained personnel should give oxygen. Get medical attention.

4.2 Most important symptoms and effects, both acute and delayed

Early symptoms of vitamin D intoxication are associated with excess blood calcium (hypercalcemia). Such symptoms include weakness, headache, drowsiness, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, metallic taste, and anorexia. Late symptoms include excessive thirst, increased urination, light sensitivity, itching, high blood pressure (hypertension), abnormal heart rate (cardiac arrhythmia), and sensory disturbances. Repeated exposure to doxercalciferol disrupts blood calcium levels and results in bone thickening, mineralization of organs and tissues, especially blood vessels, and may be fatal.

4.3 Indication of any immediate medical attention and special treatment needed

Treat symptomatically and supportively. See package insert for additional information.

5. Fire Fighting Measures

5.1 Extinguishing media

Suitable extinguishing media: All means: water, carbon dioxide, foam or dry chemical.

Unsuitable extinguishing media: Strong water jet.

5.2 Specific hazards arising from the chemical

Hazardous combustion products: Carbon monoxide, carbon dioxide.

5.3 Special Protective Equipment and Precautions for Fire-fighters

In case of fire, use full firefighting turnout (bunker) gear and self-contained breathing apparatus (SCBA). Keep personnel upwind and away from fire. Move container from fire area if you can do it without risk. Do not scatter spilled material with high-pressure water streams. Dike fire-control water for later disposal.

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6. Accidental Release Measures

6.1 Personal precautions and Protective Equipment:

Eye protection, respiratory protective equipment, and suitable protective clothing should be worn (see Section 8).

6.2 Emergency Procedures:

Follow local workplace procedures. Prevent the product from entering the environment. Avoid discharges to sewers, drains, waterways, or onto the ground.

6.3 Methods for containment:

Absorb spilled liquid with a suitable inert material, place in suitable container for disposal and mop area.

6.4 Methods for clean-up:

Wash the floor with plenty of water, absorb or retain the cleaning water for disposal.

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7. Handling and Storage

7.1 Precautions for Safe Handling

Product should be used in a controlled work area. Use with adequate ventilation. Avoid contact with eyes, skin and clothing. Place a disposable absorbent pad under the product preparation area. Do not eat, smoke or drink while handling product. Wash thoroughly after handling.

7.2 Conditions for Safe Storage

Store at 25°C (77°F): excursions permitted to 15-30°C (59-86°F).

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8. Exposure Controls/Personal Protection

8.1 Exposure Limits

Sanofi-aventis occupational exposure limit, doxercalciferol: 0.01 micrograms/m^3, 8-hour TWA.

8.2 Appropriate Engineering Controls

Provide adequate ventilation. No other specific controls are needed under normal handling conditions.

8.3 Individual Protection Measures

Eye/face protection: Safety glasses or safety goggles should be worn if there is a potential for eye contact with the product.

Skin protection: Use approved gloves if skin contact with the product is possible; double gloves are recommended. After product preparation, the outer gloves can be removed and discarded in an approved waste container and the procedure completed. Gloves should be changed when torn, punctured or contaminated. Use of a protective or disposable gown or laboratory coat is recommended if there exists a potential for contact with the product.

Respiratory protection: None normally required for routine handling of the product. However, approved respiratory protection should be worn if there is a potential for exposure to the product. A respiratory protection program that meets OSHA 29 CFR 1910.134 and ANSI Z88.2 must be followed whenever workplace conditions warrant respirator usage.

General hygiene considerations: Wash hands before breaks and at the end of the work shift.

Clinical Setting: Health care workers who prepare or administer hazardous drugs or who work in areas where these drugs are used should follow specific workplace handling guidelines in order to prevent exposure to these agents in the air or on work surfaces, clothing, medical equipment, or in patient urine or feces.

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9. Physical and Chemical Properties

Appearance: Salmon, peach or yellow oval capsules.
Odor: No data available.

Odor threshold: No data available.
pH: No data available.
Melting point/ Freezing point: No data available.
Initial boiling point/boiling point range: No data available.
Flash point: No data available.
Evaporation rate: No data available.
Flammability: No data available.
Upper/lower flammability or explosive limits: No data available.
Vapor pressure: No data available.
Vapor density: No data available.
Specific gravity: No data available.
Solubility: No data available.
Partition coefficient: n-octanol/water: No data available.
Auto-ignition temperature: No data available.
Decomposition temperature: No data available.
Viscosity: No data available.

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10. Stability and Reactivity

10.1 Reactivity

Not a reactive material under normal handling conditions.

10.2 Chemical Stability

Stable under normal handling conditions.

10.3 Possibility of hazardous reactions

None known.

10.4 Conditions to Avoid

Keep away from heat, sparks and flames.

10.5 Incompatible materials

Strong oxidizing and reducing agents.

10.6 Hazardous decomposition products

Carbon monoxide, carbon dioxide.

11. Toxicological Information

The following information is for the active ingredient doxercalciferol unless otherwise noted:

Information on likely routes of exposure: Not expected under normal handling conditions. Unintended spills or releases could result in exposure to eyes, skin and respiratory tract.

Symptoms related to the physical, chemical and toxicological characteristics: Early symptoms of vitamin D intoxication are associated with excess blood calcium (hypercalcemia). Such symptoms include weakness, headache, drowsiness, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, metallic taste, and anorexia. Late symptoms include excessive thirst, increased urination, light sensitivity, itching, high blood pressure (hypertension), abnormal heart rate (cardiac arrhythmia), and sensory disturbances.

Effects of short-term (acute) exposure: Vitamin D compounds have the potential to produce hypercalcemia. Excessive intake can be toxic, and in extreme cases fatal. The principle adverse effects include hypercalcemia, hyperphosphatemia, hypercalciuria, and oversuppression of iPTH.

Effects of long-term (chronic) exposure: Chronic hypercalcemia can lead to generalized vascular calcification of the heart and arteries, and other soft-tissue calcification. Hyperphosphatemia can exacerbate hyperparathyroidism. Hypercalciuria may accelerate the onset of renal failure through nephrocalcinosis. Oversuppression of iPTH may lead to adynamic bone syndrome.

Acute toxicity (LD50):
Oral route, rat: 1.7 – 3.5 mg/kg

Skin corrosion/irritation: May be irritating to skin.

Serious eye damage/irritation: May be irritating to eyes.

Sensitization: No data available.

Specific target organ toxicity – single exposure (STOT-SE): No data available.

Specific target organ toxicity – repeated exposure (STOT-RE): Bones, kidney, and parathyroid gland.

Carcinogenicity: Long-term studies in animals to evaluate carcinogenic potential have not been conducted.

Not listed by NTP, not found to be a potential carcinogen by IARC or OSHA.

Titanium dioxide has been classified by IARC as 2B: Possibly carcinogenic to humans. Tumors were observed at high dose in animal studies by inhalation and intratracheal administration. Tumors were not observed by other routes.

Reproductive toxicity and teratogenicity: Reproduction studies in rats and rabbits, at doses up to 20 µg/kg/day and 0.03 µg/kg/day (approximately 25 times and less than the maximum recommended therapeutic dose of 60 µg/week based on µg/m² body surface area, respectively) have revealed no teratogenic or fetotoxic effects due to doxercalciferol. No effect on male or female fertility in rats at oral doses up to 2.5 µg/kg/day.

Mutagenicity: Doxercalciferol did not cause mutations in an Ames bacterial mutagenicity assay and in a mouse lymphoma forward mutation assay. Although structural chromatid and chromosomal aberrations were seen in a human lymphocyte chromosome aberration assay, in the presence of metabolic activation only, an in vivo mouse micronucleus assay gave negative results.

Aspiration hazard: No data available.

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12. Ecological Information

The following information is for the active ingredient doxercalciferol unless otherwise noted:

12.1. Ecotoxicity

No data available.

12.2. Persistence and degradability

No data available.

12.3. Bioaccumulative potential

No data available.

12.4 Mobility in soil

No data available.

12.5 Other adverse effects

No data available.

13. Disposal Considerations

13.1 Disposal of product waste

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.

13.2 Disposal of packaging waste

Dispose of in a safe manner in accordance with federal, state and local environmental regulations. Empty packages, containers or liners may contain product residue.

14. Transport Information

14.1 Basic shipping information, finished product

U.S. DOT	Not a regulated material.
ICAO/IATA	Not a regulated material.
IMDG	Not a regulated material.

15. Regulatory Information

US Regulations
CERCLA Hazardous Substance List (40 CFR 302.4): Not listed.
Clean Water Act Section 311 Hazardous Substances (40 CFR 117.3): Not listed.
Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130): Not listed.
SARA Title III:
Section 302 Extremely Hazardous Substance (40 CFR 355, Appendix A): Not listed.
Section 313 Toxic Release Inventory (40 CFR 372): Not listed.

State Regulations
California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): Ethyl alcohol is listed but refers to its presence in alcoholic beverages.
Massachusetts Right-To-Know List: Not listed.
New Jersey Right-To-Know List: Not listed.
Pennsylvania Right-To-Know List: Not listed.

16. Other Information

Other Information: The information contained herein is based upon data considered true and accurate. Winthrop U.S. makes no warranties, express or implied, as to the adequacy of the information contained herein. This information is offered solely for the user's consideration, investigation and verification. Report to the manufacturer any allegations of health effects resulting from handling or accidental contact with this material.

Abbreviations and Acronyms
CAS: Chemical Abstracts Service
DOT: U.S. Department of Transportation
EST: Eastern standard time (U.S.)
IATA: International Air Transport Association
IMDG: International Maritime Dangerous Goods Code
LC50: Lethal concentration, 50%
LD50: Lethal dose, 50%
OEL: Occupational Exposure Limit
PPE: Personal Protection Equipment
SDS: Safety Data Sheet
STEL: Short-term exposure limit
TWA: Time-weighted average
U.S.: United States

Date Prepared : January 26, 2017

First version.