1. Product and Company Identification

PRODUCT NAME: SEVELAMER CARBONATE TABLETS

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 U.S.:	**(908) 981-5550**

Product use: Pharmaceutical product.

2. Hazards Identification

2.1 Classification in accordance with 29 CFR 1910.1200

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

Classification: Sevelamer carbonate is not classified as a hazardous substance.

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.

2.3 Hazards Not Otherwise Classified (HNOC)

Not classified.

3. Composition/Information on Ingredients

Chemical Name:	Common Name:	CAS #:	Percentage or concentration range
Poly(allylamine-co-N,N'-diallyl-1,3-diamino-2-hydroxypropane) carbonate salt	Sevelamer carbonate	845273-93-0	800 mg per tablet

Inactive Ingredients: Hypromellose, diacetylated monoglycerides, microcrystalline cellulose, sodium chloride and zinc stearate.

4. First Aid Measures

4.1 First aid procedures

Eye contact: In case of contact with dust from broken tablets or capsules, 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 broken tablets or capsules, 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 dust from broken tablets or capsules 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

In studies with healthy human volunteers, it was shown that sevelamer hydrochloride is not systemically absorbed with ingestion. Based on trials of 8 to 52 weeks in duration, the most common adverse effects were gastrointestinal reactions, including nausea, vomiting, diarrhea, dyspepsia, abdominal pain, flatulence and constipation.

4.3 Indication of any immediate medical attention and special treatment needed

Treat symptomatically and supportively.

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, oxides of nitrogen.

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.

6. Accidental Release Measures

6.1 Personal precautions and Protective Equipment:

Eye protection, respiratory protective equipment, and suitable protective clothing should be worn if significant dust emissions are generated from broken or crushed tablets or capsules.

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:

Vacuum or scoop up, moisten any dust with water before collection with a shovel or broom.

6.4 Methods for clean-up:

Place material in suitable container for disposal. Wash the floor with plenty of water, absorb or retain the cleaning water for disposal.

7. Handling and Storage

7.1 Precautions for Safe Handling

Use with adequate ventilation. Avoid breathing dust if tablets are crushed or spilled. Do not get dust in eyes or on skin. Wash thoroughly after handling.

7.2 Conditions for Safe Storage

Keep container tightly closed. Store at 25°C (77°F).

8. Exposure Controls/Personal Protection

8.1 Exposure Limits

Sanofi-aventis occupational exposure limit, sevelamer carbonate: 1 mg/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 dust exposure from broken or crushed tablets.

Skin protection: Suitable protective gloves should be worn if handling the unfinished product or broken or crushed tablets.

Respiratory protection: None normally required. Approved respiratory protection should be worn if there is a potential for exposure to dust from handling operations or from broken or crushed tablets.

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

9. Physical and Chemical Properties

Appearance: White oval film-coated tablets.
Odor: No data available.
Odor threshold: No data available.
pH (sevelamer carbonate): 8 - 10.5 (1% aqueous slurry).
Melting point/ Freezing point: Not applicable.
Initial boiling point/boiling point range: Not applicable.
Flash point: Not applicable.
Evaporation rate: Not applicable.
Flammability: Not applicable.
Upper/lower flammability or explosive limits: Not applicable. Vapor pressure: Not applicable.
Vapor density: Not applicable.
Relative density: 0.4 - 0.8 mg/ml (Sevelamer carbonate bulk).
Solubility: Insoluble in aqueous and organic solvents; hydrophilic; swells in water.
Partition coefficient: n-octanol/water: Not applicable. Insoluble in aqueous and organic solvents.
Auto-ignition temperature: No data available.
Decomposition temperature: No data available.
Viscosity: Not applicable.

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, oxides of nitrogen.

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11. Toxicological Information

The following information is for the active ingredient sevelamer carbonate unless otherwise noted. In some cases data for the salt form sevelamer hydrochloride are provided in this section, since sevelamer carbonate is expected to have a similar toxicological profile.

Information on likely routes of exposure: Exposure not expected under normal use. Dust from broken or crushed tablets could result in exposure to eyes, skin and respiratory tract.

Symptoms related to the physical, chemical and toxicological characteristics: Gastrointestinal reactions, including nausea, vomiting, diarrhea, dyspepsia, abdominal pain, flatulence and constipation.

Effects of short-term (acute) exposure: Gastrointestinal effects.

Effects of long-term (chronic) exposure: Gastrointestinal effects.

Acute toxicity (LD50):
LD50, mouse, oral: >3.2 g/kg. Preclinical and clinical studies with sevelamer carbonate indicate that it is not systemically absorbed following ingestion.

Skin corrosion/irritation: No data available.

Serious eye damage/irritation: No data available.

Sensitization: No data available.

Specific target organ toxicity – single exposure (STOT-SE): Not classified. In single dose pharmacology studies at doses up to 2000 mg/kg, a different salt, sevelamer hydrochloride, produced no neurological or behavioral changes in mice or cardiovascular or gastrointestinal effects in dogs.

Specific target organ toxicity – repeated exposure (STOT-RE): Not classified.
Sevelamer carbonate: Up to 4500 mg/kg/day, rat (male), oral, 28 days, well tolerated.
NOAEL: 761 mg/kg/day. ≥1000 mg/kg/day, increased urinary electrolyte excretion.
Sevelamer carbonate: 1000 and 200 mg/kg/day, dogs, well tolerated, emaciated appearance.

Carcinogenicity: Not classified. In lifetime carcinogenicity bioassays in rats and mice given sevelamer hydrochloride in the diet, doses of 3 g/kg/day caused an increase in urinary bladder transitional cell hyperplasia, papillomas and carcinomas in male rats. These changes are considered to be the result of inflammatory responses to abnormal crystalline deposits in the urine and mineral imbalances and are not considered a carcinogenic effect of sevelamer hydrochloride. In mice, there was no increase in tumor incidence at 9 g/kg/day, the maximum dose tested.

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

Reproductive toxicity and teratogenicity: Not classified. In pregnant rats given doses of sevelamer hydrochloride during organogenesis, reduced or irregular ossification of fetal bones, probably due to a reduced absorption of fat-soluble vitamin D, occurred at a dose approximately equal to the maximum clinical trial dose of 13 g on a body surface area basis. In pregnant rabbits given oral doses of sevelamer hydrochloride by gavage during organogenesis, an increase of early resorptions occurred at dose approximately twice the maximum clinical trial dose on a body surface area basis. Sevelamer hydrochloride did not impair the fertility of male or female rats.

Mutagenicity: Not classified. Ames microbial mutagenicity assay: negative
in vitro chromosome aberration assay with metabolic activation: weakly positive
in vivo mouse micronucleus test: negative.

Aspiration hazard: Not applicable.

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12. Ecological Information

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

12.1. Ecotoxicity

Harmful to aquatic life with long lasting effects.

LC50, crustacean/water flea (Daphnia magna Straus), 48 hours: >1000 mg/L
LC50, fish (rainbow trout), 96 hours: 82 mg/L (based on Sevelamer hydrochloride)
LC50, green algae (Pseudokirchnerellia subcapita), 72 hours: 63 mg/L

12.2. Persistence and degradability

Biological degradability: Biodegradation test (OECD 301) showed no net biodegradation over a 28 day period.

12.3. Bioaccumulative potential

Potential to bioaccumulate, based on physical properties and lack of biodegradability.

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.
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): Not listed.
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., a business of Sanofi 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

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First version.