1. Product and Company Identification

PRODUCT NAME: MULTAQ® (dronedarone) Tablets
400 mg

Substance name: Dronedarone hydrochloride

Supplier:
Sanofi-aventis U.S. LLC
A SANOFI COMPANY
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

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, dronedarone hydrochloride:

Classification:
Eye damage/irritation, Category 2A

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, dronedarone hydrochloride:

Signal Word: Warning

Hazard Statement(s): Causes serious eye irritation

Symbol(s): Exclamation mark

Precautionary Statement(s):

- Prevention: Wash hands thoroughly after handling. Wear eye protection (see Section 8).
- Response: If in eyes: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical attention.
- Storage: Store in a well-ventilated place. Keep container tightly closed.
- Disposal: Disposal should be in accordance with applicable regional, national and local laws and regulations.

2.3 Hazards Not Otherwise Classified (HNOC)

No information available.

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3. Composition/Information on Ingredients

Chemical Name:	**Common Name:**	**CAS #:**	**Percentage or concentration range**
N-{2-butyl-3-[4-(3-dibutylaminopropoxy) benzoyl]benzofuran-5-yl} methanesulfonamide, hydrochloride	Dronedarone hydrochloride	141625-93-6	400 mg per tablet

Inactive Ingredients: Hypromellose, starch, crospovidone, poloxamer 407, lactose monohydrate, colloidal silicon dioxide, magnesium stearate.

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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

Dizziness, fall in blood pressure, slowing of the pulse. Most common adverse reactions (≥2%) in clinical trials were diarrhea, nausea, abdominal pain, vomiting, and asthenia.

4.3 Indication of any immediate medical attention and special treatment needed

Treat symptomatically and supportively.

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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 sulfur and 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. Protect from light. Store in a cool, well-ventilated area. Store at 25°C (77°F): excursions permitted to 15–30°C (59–86°F).

8. Exposure Controls/Personal Protection

8.1 Exposure Limits

Sanofi-aventis occupational exposure limit, dronedarone hydrochloride: 0.1 mg/m^3, 8-hour TWA.

8.2 Appropriate Engineering Controls

Provide adequate ventilation. No other specific controls are needed under normal handling conditions. If the integrity of the tablets is compromised (cutting, crushing, or unintended breakage), then handling within a ventilated control device is recommended. If handled outside of a ventilated control device, appropriate respiratory protection should be used.

8.3 Individual Protection Measures

Eye/face protection: None normally required. 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 for routine handling. If the integrity of the tablets is compromised (cutting, crushing, or unintended breakage), then double gloves are recommended.

Respiratory protection: None normally required. If the integrity of the tablets is compromised (cutting, crushing, or unintended breakage), then handling within a ventilated control device is recommended. If handled outside of a ventilated control device, appropriate approved respiratory protection should be used.

General hygiene considerations: Suitable work clothes. If the integrity of the tablets is compromised (cutting, crushing, or unintended breakage), then a protective gown is recommended. Wash hands before breaks and at the end of the work shift.

9. Physical and Chemical Properties

Appearance: White, oblong film-coated tablets.
Odor: No data available.
Odor threshold: No data available.
pH: No data available.
Melting point (dronedarone hydrochloride): 137 - 145 ^{o}C
Initial boiling point/boiling point range: Not applicable.
Flash point: Not applicable.
Evaporation rate: Not applicable.
Flammability: No data available.

Upper/lower flammability or explosive limits: Not applicable.
Vapor pressure: Not applicable.
Vapor density: Not applicable.
Relative density: No data available.
Solubility in water: 0.64 g/l at 25 °C (practically insoluble in water)
Partition coefficient: n-octanol/water (dronedarone hydrohloride): Log Kow = 4.63 at pH=7
Auto-ignition temperature: No data available.
Decomposition temperature (dronedarone hydrochloride): 160 °C; Method: under oxygen
Viscosity: Not applicable.

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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, oxides of sulfur and nitrogen.

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11. Toxicological Information

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

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: Most common adverse reactions (≥2%) in clinical trials were diarrhea, nausea, abdominal pain, vomiting, and asthenia

Effects of short-term (acute) exposure: Fall in blood pressure, slowing of the pulse.

Effects of long-term (chronic) exposure: No data available.

Acute toxicity (LD50):
Oral route, rat: > 2,000 mg/kg.

Skin corrosion/irritation: Not irritating in animal studies.

Serious eye damage/irritation: Serious eye irritant based on animal studies.

Sensitization: Not a dermal sensitizer based the Local Lymph Node Assay (LLNA).

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

Specific target organ toxicity – repeated exposure (STOT-RE): Rat: No observed effect level (6 months): approximately 10 mg/kg/day (oral route).

Carcinogenicity: In studies in which dronedarone was administered to rats and mice for up to 2 years at doses of up to 70 mg/kg/day and 300 mg/kg/day, respectively, there was an increased incidence of histiocytic sarcomas in dronedarone-treated male mice (300 mg/kg/day or 5× the maximum recommended human dose based on AUC comparisons), mammary adenocarcinomas in dronedarone-treated female mice (300 mg/kg/day or 8× MRHD based on AUC comparisons) and hemangiomas in dronedarone-treated male rats (70 mg/kg/day or 5× MRHD based on AUC comparisons).

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

Reproductive toxicity and teratogenicity:
Rat: Dronedarone was studied at dosages of 0, 10, 30 or 100 mg/kg/day from Day 6 to Day 15 of gestation in groups of 22 mated females. Dronedarone induced at 100 mg/kg/day maternal toxicity characterized by reduced body weight and food intake during the treatment period. At this dose, marked effects were observed on embryo-fetal development such as increased post-implantation losses, reduced fetal and placenta weights, various external, visceral and skeletal malformations in most of the fetuses. At lower dose levels (10 and 30 mg/kg/day), Dronedarone had no adverse effects either on the mothers or their litters.

Rabbit: Dronedarone was studied at dose levels of 0, 20, 60 or 200 mg/kg/day of Dronedarone from Day 6 to Day 18 of gestation in groups of 22 mated females. Dronedarone induced deaths, abortion and marked weight loss at 200 mg/kg/day to dams and a slight reduction of body-weight gain soon after dosing started at 60 mg/kg/day. The maternal NOEL was considered to be 20 mg/kg/day. The fetal no-observed-effect-level was 200 mg/kg/day.

Mutagenicity: Dronedarone did not demonstrate genotoxic potential in the in vivo mouse micronucleus test, the Ames bacterial mutation assay, the unscheduled DNA synthesis assay, or an in vitro chromosomal aberration assay in human lymphocytes. S-9 processed dronedarone, however, was positive in a V79 transfected Chinese hamster V79 assay.

Aspiration hazard: Not applicable.

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12. Ecological Information

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

12.1. Ecotoxicity

Acute aquatic toxicity, Category 1
Chronic aquatic toxicity, Category 1
Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Fish toxicity (LC50): 0.45 mg/l
Species: Oncorhynchus mykiss
Exposure duration: 96 h

Toxicity on invertebrates (EC50): > 0.43 mg/l
Species: Daphnia magna
Exposure duration: 48 h

Algae toxicity (EbC50): 0.012 mg/l
Species: Pseudokirchneriella subcapitata
Exposure duration: 72 h

Algae toxicity (ErC50): 0.045 mg/l
Species: Pseudokirchneriella subcapitata
Exposure duration: 72 h

12.2. Persistence and degradability

Biological degradability: 23.8 %
Testing period: 29 d
Method: OECD 302 B
The product is not readily biodegradable according to OECD criteria.

12.3. Bioaccumulative potential

Bioconcentration factor (BCF): 95 - 134
Species: Lepomis macrochirus (Bluegill sunfish)
Potentially bioaccumulable in living organisms.

12.4 Mobility in soil

No data available.

12.5 Other adverse effects

No data available.

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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.

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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.

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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.

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16. Other Information

Dronedarone hydrochloride is included in the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016.

Other Information: The information contained herein is based upon data considered true and accurate. Sanofi-aventis U.S. LLC. 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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Second version.