1. Product and Company Identification

PRODUCT NAME: JEVTANA® (cabazitaxel) Injection
60 mg/1.5 mL

Substance name: Cabazitaxel; XRP6258

This product consists of Cabazitaxel (about 4 %) and polysorbate 80 in glass vials, with parallel vials of diluent containing approximately 13 % ethanol in water.

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. Antineoplastic agent.

2. Hazards Identification

2.1 Classification in accordance with 29 CFR 1910.1200

JEVTANA (CABAZITAXEL) VIAL:

Classification:
Acute toxicity, Category 3
Acute toxicity, Category 4
Skin irritation, Category 2
Germ cell mutagenicity, Category 2
Reproductive toxicity, Category 1B
Effects on or via lactation
Specific target organ toxicity - repeated exposure, Category 1

DILUENT (13% ETHYL ALCOHOL) VIAL:

Classification:
Flammable liquid, Category 3

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 individual vials:

JEVTANA (CABAZITAXEL) VIAL:

Signal Word: Danger

Hazard Statement(s): May damage the unborn child. Harmful if swallowed. Toxic in contact with skin. Causes skin irritation. Suspected of causing genetic defects. May damage the unborn child. Suspected of damaging fertility. May cause harm to breast-fed children. Causes damage to organs through prolonged or repeated exposure.

Symbol(s): Health Hazard; Skull and Crossbones

Precautionary Statement(s):

- Prevention: Obtain special instructions before use. Do not breathe dust. Wear protective gloves and protective clothing. Avoid contact during pregnancy and while nursing.
- Response: IF exposed: Call a POISON CENTER or doctor.
- Storage: Store in a well-ventilated place. Keep container tightly closed. Store locked up.
- Disposal: Dispose of contents in accordance with applicable regional, national and local laws and regulations.

DILUENT (13% ETHYL ALCOHOL) VIAL:

Signal Word: Warning

Hazard Statement(s): Flammable liquid and vapor.

Symbol(s): Health Hazard: Flame

Precautionary Statement(s):

- Prevention: Keep away from heat and open flame. No smoking. Keep container tightly closed. Wear protective gloves and eye protection.
- Response: In case of fire: use all means (water, carbon dioxide, foam or dry chemical) to extinguish. If on skin or hair: Take off immediately all contaminated clothing. Rinse skin with water.

- Storage: Store in a well-ventilated place. Keep cool.

- Disposal: Dispose of contents 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

This product consists of Cabazitaxel (about 4 %) and polysorbate 80 in a glass vial with a parallel vial of diluent containing 13 % ethanol in water.

Jevtana vial:

Chemical Name:	**Common Name:**	**CAS #:**	**Percentage or concentration range**
(2α,5β,7β,10β,13α)-4-acetoxy-13-({(2R,3S)-3-[(tertbutoxycarbonyl) amino]-2-hydroxy-3-phenylpropanoyl}oxy)-1-hydroxy-7,10-dimethoxy-9-oxo-5,20-epoxytax-11-en-2-yl benzoate – propan-2-one(1:1).	Cabazitaxel	183133-96-2	40 mg/mL (4%)
Polyoxyethylene 20 sorbitan monooleate	Polysorbate 80	9005-55-6	1.04 g/mL

Diluent vial:

Chemical Name:	**Common Name:**	**CAS #:**	**Percentage or concentration range**
Ethyl alcohol	Alcohol	64-17-5	13 %
Water	Water	7732-18-5	87 %

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 immediately.

4.2 Most important symptoms and effects, both acute and delayed

The most common symptoms and adverse reactions in clinical trials included anemia, leukopenia, neutropenia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, asthenia, abdominal pain, hematuria, back pain, anorexia, peripheral neuropathy, pyrexia, dyspnea, dysguesia, cough, arthralgia, and alopecia.

4.3 Indication of any immediate medical attention and special treatment needed

Treat symptomatically and supportively. Refer to 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, 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.

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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:

Small Spills

If a small spill occurs within a ventilated cabinet, wear protective equipment to prevent inhalation or eye/skin contact (see Section 8). Wipe up spill with absorbent material and place in an impervious container.

Large Spills

During a large spill, evacuate non-essential personnel from the area. Wear protective equipment to prevent inhalation or eye/skin contact (see Section 8). Absorb the liquid with an inert absorbent material (e.g. absorbent pad, clay, vermiculite, etc.). Avoid excessive physical disturbance of spill during cleanup to minimize aerosol generation.

6.3 Methods for containment:

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

6.4 Methods for clean-up:

Wash the floor with dilute bleach and plenty of water, absorb or retain the cleaning water for disposal. Carefully place the waste in a labeled receptacle for safe disposal as a contaminated waste. Remove any contaminated clothing, personal protective equipment and barrier sheeting, and place in a double sealed, labeled waste container marked for disposal. Wash skin thoroughly after handling.

7. Handling and Storage

7.1 Precautions for Safe Handling

Product should be used in a controlled work area. Use with adequate ventilation (see Section 8). Avoid contact with eyes, skin and clothing. To minimize hazards from accidental breakage or spills of containers and to simplify clean-up, store and transport within secondary containers, pans or trays. Use disposable protective coatings and/or barrier sheeting in use areas where possibility of spillage exists to simplify cleanup. Do not eat, smoke or drink while handling product. Wash hands thoroughly after handling.

7.2 Conditions for Safe Storage

This product should be stored in a closed secondary container that minimizes the risk of breakage. Protect from light. Store in a cool, well-ventilated area. Store at 25°C (77°F); excursions permitted between 15°–30°C (59°–86°F). Do not refrigerate.

8. Exposure Controls/Personal Protection

8.1 Exposure Limits

Sanofi-aventis occupational exposure limit, cabazitaxel: 0.1 micrograms/m^3, 8-hour TWA.

Ethyl alcohol: OSHA PEL: 1,000 ppm. ACGIH TLV-STEL: 1,000 ppm. NIOSH REL: 1,000 ppm TWA.

8.2 Appropriate Engineering Controls

General Controls for Clinical Setting

A workplace risk assessment must be carried out in order to determine the correct engineering control measures, work practices and personal protective equipment.

Engineering Controls: Preparation of this product should be done in an area that is devoted solely to the preparation of hazardous drugs and is restricted to authorized personnel. This product should be prepared within a ventilated cabinet designed to protect workers and adjacent personnel from exposure. Transfers from primary packaging such as vials to dosing equipment should also be performed within a ventilated cabinet. Use closed-system, drug-transfer devices, glove bags and needleless systems within the ventilated cabinet. The final prepared product should be sealed in a plastic bag or other sealable container prior to removal from the cabinet. All waste containers in the cabinet should be sealed and wiped prior to removal for disposal.

8.3 Individual Protection Measures

Eye/face protection: At a minimum, safety glasses with side shields should be worn. Wear a face shield to avoid splash incidents involving the eyes, nose and mouth when adequate engineering controls are not available.

Skin protection: Use two pairs of approved chemotherapy gloves with the outer one covering the gown cuff at all times, including when unpacking product shipments. Gloves should be changed every 30 minutes or when torn, punctured or contaminated and discarded immediately in the appropriate container. When working in a ventilated cabinet, the outer gloves should be removed and bagged for disposal inside the ventilated cabinet. Avoid skin contact by using a disposable gown made of non-linting and non-absorbent fabric. The gown should have a closed front, long sleeves and elastic or knit closed cuffs and should not be reused.

Respiratory protection: Respiratory protective equipment can only be used in place of engineering controls as a temporary measure in emergency situations or when control by other means is not feasible. Respiratory protection must be selected according to the risk from the work task or situation. In general, positive pressure, supplied air respiratory protective equipment (hood, half suit or full suit), which provides high factors of protection, is used when there is risk of airborne exposure above recommended exposure levels. All respiratory protection should be in compliance with the OSHA Respiratory Protection Standard, 29 CFR 1910.134, or other regulations applicable to the country of use.

General hygiene considerations: 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. Wash hands with soap and water immediately before using personal protective clothing (such as disposable gloves and gowns) and after removing personal protective clothing, including gloves. Outer gloves and gowns should be removed and bagged for disposal in the appropriate container at the site of administration. The waste container should be double-bagged before removal of the inner gloves. Clean and decontaminate work areas before and after each activity and at the end of each shift. See Section 13 for guidance on waste handling.

Detailed advice can be found in published guidance on the handling of oncolytic and cytotoxic agents. See Section 16.

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9. Physical and Chemical Properties

Jevtana vial:
Appearance: Clear yellow to brownish-yellow viscous solution.
Odor: No data available.
Odor threshold: No data available.
pH: No data available.
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: Not applicable.
Vapor density: Not applicable.
Relative density: No data available.
Solubility: No data available.
Partition coefficient: n-octanol/water (cabazitaxel): Log Kow = 3.88; computed value (QSAR).
Auto-ignition temperature: No data available.
Decomposition temperature: No data available.
Viscosity: No data available.

Diluent vial:
Appearance: Clear, colorless solution.
Odor: No data available.
Odor threshold: No data available.
pH: No data available.
Freezing point: No data available.
Initial boiling point/boiling point range: No data available.
Flash point: (13% ethanol-water mixture): 45 – 50 ^{o}C (113 – 122 ^{o}F)
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.
Relative density: 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. 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, oxides of nitrogen.

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11. Toxicological Information

The following information is for the active ingredient cabazitaxel 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: The most common symptoms and adverse reactions in clinical trials included diarrhea, fatigue, nausea, vomiting, constipation, asthenia, abdominal pain, back pain, cough, and alopecia.

Effects of short-term (acute) exposure: The most common symptoms and adverse reactions in clinical trials included anemia, leukopenia, neutropenia, thrombocytopenia, hematuria, anorexia, peripheral neuropathy, pyrexia, dyspnea, dysguesia, and arthralgia.

Effects of long-term (chronic) exposure: May be carcinogenic due to the pharmacological activity. If the compound is bioavailable via the route of exposure and exposure occurs for prolonged periods of time, due to the pharmacological activity it is presumed that potentially adverse and irreversible effects could occur, including limited carcinogenic and reprotoxic effects.

Acute toxicity (LD50):
Oral route, rat: 500 mg/kg.
May be toxic in contact with skin.

Skin corrosion/irritation: Strong skin irritant based on animal studies.

Serious eye damage/irritation: not an eye irritant based on in vitro tests.

Sensitization: No data available.

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

Specific target organ toxicity – repeated exposure (STOT-RE): Causes damage to organs through prolonged or repeated exposure.

Carcinogenicity: Long-term animal studies have not been performed to evaluate the carcinogenic potential of cabazitaxel. Not listed by NTP, not found to be a potential carcinogen by IARC or OSHA.

Reproductive toxicity and teratogenicity: Non-clinical studies in rats and rabbits have shown that cabazitaxel is embryotoxic, fetotoxic, and abortifacientat at exposures significantly lower than those expected at the recommended human dose level. Cabazitaxel was shown to cross the placenta barrier within 24 hours of a single intravenous administration of a 0.08 mg/kg dose (approximately 0.02 times the maximum recommended human dose-MRHD) to pregnant rats at gestational day 17. Cabazitaxel administered once daily to female rats during organogenesis at a dose of 0.16 mg/kg/day (approximately 0.02–0.06 times the Cmax in patients with cancer at the recommended human dose) caused maternal and embryofetal toxicity consisting of increased post-implantation loss, embryolethality, and fetal deaths. Decreased mean fetal birth weight associated with delays in skeletal ossification were observed at doses ≥ 0.08 mg/kg (approximately 0.02 times the Cmax at the MRHD). In utero exposure to cabazitaxel did not result in fetal abnormalities in rats or rabbits at exposure levels significantly lower than the expected human exposures.

Cabazitaxel may impair fertility in humans. In a fertility study performed in female rats at cabazitaxel doses of 0.05, 0.1, or 0.2 mg/kg/day there was no effect of administration of the drug on mating behavior or the ability to become pregnant.

Mutagenicity: Cabazitaxel was positive for clastogenesis in the in vivo micronucleus test, inducing an increase of micronuclei in rats at doses ≥ 0.5 mg/kg. Cabazitaxel increased numerical aberrations with or without metabolic activation in an in vitro test in human lymphocytes though no induction of structural aberrations was observed. Cabazitaxel did not induce mutations in the bacterial reverse mutation (Ames) test. The positive in vivo genotoxicity findings are consistent with the pharmacological activity of the compound (inhibition of tubulin depolymerization).

Aspiration hazard: No information available.

Information for the ingredient Polysorbate 80:

Acute oral toxicity LD50 (rat): 25,000 mg/kg

Irritation: Mild eye irritant. Mild skin irritant.

Information for Ethyl alcohol:

Acute oral toxicity: LD50 (rat): 7.060 mg/kg
Acute inhalation toxicity: LC50 (rat, 4 h): 95.6 mg/l
Acute dermal toxicity: LD50 (rabbit): > 20,000 mg/kg

12. Ecological Information

The following information is for the active ingredient cabazitaxel 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. Wastes should be double contained (e.g. double sealed bags) and labeled indicating contents to ensure safe handling and disposal. Incineration of waste product is recommended.

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): 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

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

References

1. NIOSH Alert: Preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings. 2004. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004–165.

2. OSHA Technical Manual, TED 1-0.15A, Section VI: Chapter 2. Controlling Occupational Exposure to Hazardous Drugs. OSHA, 1999.

3. American Society of Health-System Pharmacists. (2006) ASHP Guidelines on Handling Hazardous Drugs.

4. Polovich, M., White, J. M., & Kelleher, L.O. (eds.) 2005. Chemotherapy and biotherapy guidelines and recommendations for practice (2nd. Ed.) Pittsburgh, PA: Oncology Nursing Society.

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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Third version.