Dear Healthcare Professional:

Sanofi-aventis U.S. is informing you about two important changes to the way that Taxotere® (docetaxel) Injection Concentrate vials are being provided for your use:

1. **New single vial formulation:** The new **1-vial Taxotere® at a doubled concentration is now replacing the current 2-vial Taxotere® packaging.** The new 1-vial concentration is 20 mg/mL in comparison to the previous 2-vial preparation, which was 10 mg/mL.

2. **No reconstitution needed:** The new 1-vial Taxotere® **no longer requires reconstitution**. Taxotere® can now be withdrawn from the new 1-vial formulation and injected directly into the IV infusion solution without further dilution.

Administration Precautions
Taxotere® is a cytotoxic anticancer drug and, as with other potentially toxic compounds, caution should be exercised when handling and preparing Taxotere® solutions. The use of gloves is recommended.

If Taxotere® Injection Concentrate, initial diluted solution, or final dilution for infusion should come into contact with the skin, immediately and thoroughly wash with soap and water. If Taxotere® Injection Concentrate, initial diluted solution, or final dilution for infusion should come into contact with mucosa, immediately and thoroughly wash with water.

Contact of the Taxotere® concentrate with plasticized PVC equipment or devices used to prepare solutions for infusion is not recommended. In order to minimize patient exposure to the plasticizer DEHP (di-2-ethylhexyl phthalate), which may be leached from PVC infusion bags or sets, the final Taxotere® dilution for infusion should be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets.

One-vial TAXOTERE (Injection Concentrate)
TAXOTERE Injection Concentrate requires NO prior dilution with a diluent and is ready to add to the infusion solution.
Please follow the preparation instructions provided below.

Preparation and Administration
DO NOT use the two-vial formulation (Injection Concentrate and diluent) with the one-vial formulation.

One-vial TAXOTERE (Injection Concentrate)
TAXOTERE Injection Concentrate (20 mg/mL) requires NO prior dilution with a diluent and is ready to add to the infusion solution.

1. Taxotere® vials should be stored between 2 and 25°C (36 and 77°F). If the vials are stored under refrigeration, allow the appropriate number of vials of Taxotere® Injection Concentrate vials to stand at room temperature for approximately 5 minutes before use.

2. Aseptically withdraw the required amount of Taxotere® (20 mg docetaxel/mL) with a calibrated syringe and inject into a 250 mL infusion bag or bottle of either 0.9% Sodium Chloride solution or 5% Dextrose solution to produce a final concentration of 0.3 mg/mL to 0.74 mg/mL. If a dose greater than 200 mg of Taxotere® is required, use a larger volume of the infusion vehicle so that a concentration of 0.74 mg/mL Taxotere® is not exceeded

Please see important safety information on pages 3-5 and accompanying full prescribing information, including boxed **WARNING.**

3. Thoroughly mix the infusion by gentle manual rotation.

4. As with all parenteral products, Taxotere® (docetaxel) Injection Concentrate should be inspected visually for particulate matter or discoloration prior to administration whenever the solution and container permit. If the Taxotere® dilution for intravenous infusion is not clear or appears to have precipitation, it should be discarded.

The Taxotere® dilution for infusion should be administered intravenously as a 1-hour infusion under ambient room temperature (below 25°C) and lighting conditions.

Stability
Taxotere® final dilution for infusion, if stored between 2°C and 25°C (36°F and 77°F) is stable for 4 hours. Taxotere® final dilution for infusion (in either 0.9% Sodium Chloride solution or 5% Dextrose solution) should be used within 4 hours (including the 1 hour intravenous administration).

DOSAGE FORMS AND STRENGTHS

<u>One-vial TAXOTERE (Injection Concentrate)</u>

TAXOTERE 80 mg/4 mL
TAXOTERE (docetaxel) Injection Concentrate 80 mg/4 mL: 80 mg docetaxel in 4 mL 50/50 (v/v) ratio polysorbate 80/dehydrated alcohol.

TAXOTERE 20 mg/mL
TAXOTERE (docetaxel) Injection Concentrate 20 mg/1 mL: 20 mg docetaxel in 1 mL in 50/50 (v/v) ratio polysorbate 80/dehydrated alcohol.

Important Safety Information for Taxotere®
The most common adverse reactions across all Taxotere® indications are infections, neutropenia, anemia, febrile neutropenia, hypersensitivity, thrombocytopenia, neuropathy, dysgeusia, dyspnea, constipation, anorexia, nail disorders, fluid retention, asthenia, pain, nausea, diarrhea, vomiting, mucositis, alopecia, skin reactions and myalgia.

Sanofi-aventis U.S. is committed to ensuring patient safety. Since there may be a temporary period when both formulations are available simultaneously, **please exercise caution by ensuring that all healthcare professionals who prepare and administer chemotherapeutics in your organization are aware of this concentration change.**

Please see additional important safety information on pages 3–5 and accompanying full prescribing information, including boxed **WARNING**.

Any medication errors and/or adverse events involving a sanofi-aventis U.S. product should be reported immediately to:

sanofi-aventis U.S.
Phone: (800) 633-1610 (option 2)
Fax: (908) 981-7894
E-mail: USPVmailbox@sanofi-aventis.com

Or FDA's MedWatch reporting system
Phone: 1-800-FDA-1088
Fax: 1-800-FDA-0178
Online: http://www.accessdata/fda/gov/scripts/medwatch
Mail (using the Form 3500 at MedWatch):
FDA Safety Information and
Adverse Event Reporting Program
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20852-9787

Taxotere® (docetaxel) Injection Concentrate is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.

Taxotere® in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.

Taxotere® as a single agent is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based chemotherapy.

Taxotere® in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic non-small cell lung cancer who have not previously received chemotherapy for this condition.

Taxotere® in combination with prednisone is indicated for the treatment of patients with androgen-independent (hormone-refractory) metastatic prostate cancer.

Taxotere® in combination with cisplatin and fluorouracil is indicated for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.

Taxotere® in combination with cisplatin and fluorouracil is indicated for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck.

Important Safety Information for Taxotere® (docetaxel) Injection Concentrate

WARNING

- The incidence of treatment-related mortality associated with Taxotere® therapy is increased in patients with abnormal liver function, in patients receiving higher doses, and in patients with non-small cell lung carcinoma and a history of prior treatment with platinum-based chemotherapy who receive Taxotere® as a single agent at a dose of 100 mg/m^2
- Taxotere® should not be given to patients with bilirubin > upper limit of normal (ULN), or to patients with AST and/or ALT > 1.5 × ULN concomitant with alkaline phosphatase > 2.5 × ULN

Please see additional important safety information on pages 3–5 and accompanying full prescribing information, including boxed **WARNING**.

Important Safety Information for Taxotere® (docetaxel) Injection Concentrate (continued)

- Patients with elevations of bilirubin or abnormalities of transaminase concurrent with alkaline phosphatase are at increased risk for the development of grade 4 neutropenia, febrile neutropenia, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity, and toxic death
- Patients with isolated elevations of transaminase > 1.5 × ULN also had a higher rate of febrile neutropenia grade 4 but did not have an increased incidence of toxic death
- Bilirubin, AST or ALT, and alkaline phosphatase values should be obtained prior to each cycle of Taxotere® therapy

- Taxotere® therapy should not be given to patients with neutrophil counts of <1500 cells/mm^3
  - In order to monitor the occurrence of neutropenia, which may be severe and result in infection, frequent blood-cell counts should be performed on all patients receiving Taxotere®
- Severe hypersensitivity reactions characterized by generalized rash/erythema, hypotension and/or bronchospasm, or very rarely fatal anaphylaxis, have been reported in patients who received a 3-day dexamethasone premedication
  - Hypersensitivity reactions require immediate discontinuation of Taxotere® infusion and administration of appropriate therapy
- Taxotere® must not be given to patients who have a history of severe hypersensitivity reactions to Taxotere® or to other drugs formulated with polysorbate 80
- Severe fluid retention occurred in 6.5% (6/92) of patients despite use of a 3-day dexamethasone premedication regimen. It was characterized by one or more of the following events: poorly tolerated peripheral edema, generalized edema, pleural effusion requiring urgent drainage, dyspnea at rest, cardiac tamponade, or pronounced abdominal distention (due to ascites)

- Neutropenia (<2000 neutrophils/mm^3) occurs in virtually all patients given 60–100 mg/m^2 of Taxotere® and grade 4 neutropenia (<500 cells/mm^3) occurs in 85% of patients given 100 mg/m^2 and 75% of patients given 60 mg/m^2
- Patients should be premedicated with oral corticosteroids prior to each Taxotere® administration to reduce the incidence and severity of fluid retention. Patients with pre-existing effusions should be closely monitored from the first dose for possible exacerbation of the effusions
- Treatment-related acute myeloid leukemia (AML) or myelodysplasia has occurred in patients given anthracyclines and/or cyclophosphamide, including use with Taxotere® in **adjuvant therapy** of breast cancer
- Localized erythema of the extremities with edema followed by desquamation has been observed
  - In case of severe skin toxicity, an adjustment in dosage is recommended
- Severe neurosensory symptoms (e.g. paresthesia, dysesthesia, pain) were observed in 5.5% (53/965) of **metastatic breast cancer** patients, and resulted in treatment discontinuation in 6.1%
  - When these symptoms occur, dosage must be adjusted; if symptoms persist, treatment should be discontinued

Please see additional important safety information on pages 3–5 and accompanying full prescribing information, including boxed **WARNING**.

Important Safety Information for Taxotere® (docetaxel) Injection Concentrate (continued)

- Severe asthenia was reported in 14.9% (144/965) of **metastatic breast cancer** patients, but led to treatment discontinuation in only 1.8%
    - Symptoms of fatigue and weakness may last a few days up to several weeks and may be associated with deterioration of performance status in patients with progressive disease
- Taxotere® can cause fetal harm when administered to pregnant women. Women of childbearing potential should be advised to avoid becoming pregnant during therapy with Taxotere®
- The most common adverse reactions across all Taxotere® indications are infections, neutropenia, anemia, febrile neutropenia, hypersensitivity, thrombocytopenia, neuropathy, dysgeusia, dyspnea, constipation, anorexia, nail disorders, fluid retention, asthenia, pain, nausea, diarrhea, vomiting, mucositis, alopecia, skin reactions and myalgia
- In patients treated with TCF for gastric cancer, the incidence of serious adverse events was higher in patients ≥65 years than in younger patients. Adverse events (all grades) occurring at rates ≥ 10% higher in elderly patients included lethargy, stomatitis, diarrhea, dizziness, edema, and febrile neutropenia/neutropenic infection
- Taxotere® should be administered in a facility equipped to manage possible complications (e.g. anaphylaxis)

Please see accompanying full prescribing information, including boxed **WARNING**.

Thank you for your diligence related to this matter. For additional information about Taxotere® (docetaxel) Injection Concentrate, please call sanofi-aventis U.S. Medical Information Services at (800) 633-1610 and refer to the enclosed full prescribing information, including boxed **WARNING**.

Sincerely,

Paul Chew, MD
Chief Science Officer/Chief Medical Officer
US Medical Affairs
sanofi-aventis U.S.

Enclosure:
Taxotere (docetaxel) Injection Concentrate full Prescribing Information

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