Beizray
(docetaxel) injection,
for intravenous use

zydus Pharmaceuticals USA

Beizray™ Drug Preparation Guide

The first and only FDA approved Docetaxel + Albumin kit*

*Beizray (docetaxel) injection also supplied as single dose vials

INDICATIONS

BEIZRAY is a microtubule inhibitor indicated for:

- **Breast Cancer (BC):** single agent for locally advanced or metastatic BC after chemotherapy failure; and with doxorubicin and cyclophosphamide as adjuvant treatment of operable node-positive BC
- **Non-small Cell Lung Cancer (NSCLC):** single agent for locally advanced or metastatic NSCLC after platinum therapy failure; and with cisplatin for unresectable, locally advanced or metastatic untreated NSCLC
- **Castration-Resistant Prostate Cancer (CRPC):** with prednisone in metastatic castration-resistant prostate cancer
- **Gastric Adenocarcinoma (GC):** with cisplatin and fluorouracil for untreated, advanced GC, including the gastroesophageal junction
- **Squamous Cell Carcinoma of the Head and Neck (SCCHN):** with cisplatin and fluorouracil for induction treatment of locally advanced SCCHN

WARNING: TOXIC DEATHS, HEPATOTOXICITY, NEUTROPENIA, HYPERSENSITIVITY REACTIONS, and FLUID RETENTION

See full prescribing information for complete boxed warning.

- Treatment-related mortality increases with abnormal liver function, at higher doses, and in patients with NSCLC and prior platinum-based therapy receiving Beizray at 100 mg/m^2
- Avoid use of Beizray if bilirubin > ULN, or if AST and/or ALT >1.5 × ULN concomitant with alkaline phosphatase >2.5 × ULN. LFT elevations increase risk of severe or life-threatening complications. Obtain LFTs before each treatment cycle
- Do not administer Beizray to patients with neutrophil counts <1500 cells/mm^3. Obtain frequent blood counts to monitor for neutropenia
- Severe hypersensitivity, including fatal anaphylaxis, has been reported in patients who received dexamethasone premedication. Severe reactions require immediate discontinuation of Beizray and administration of appropriate therapy
- Contraindicated if history of severe hypersensitivity reactions to docetaxel
- Severe fluid retention may occur despite dexamethasone

Do not substitute Beizray for or with other docetaxel products because Beizray has different administration instructions from other docetaxel products.

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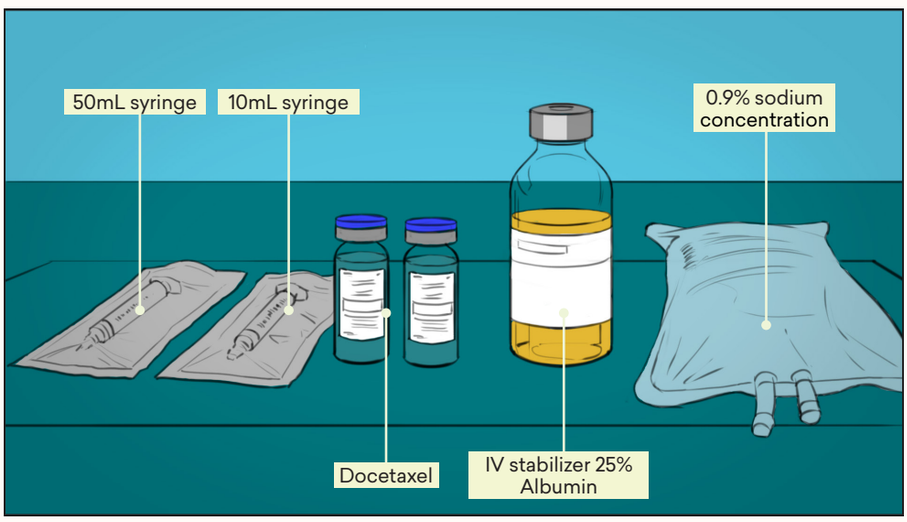
BEIZRAY™
Drug Preparation Guide

For use by healthcare professionals only. This material is intended to support the safe preparation of BEIZRAY and is consistent with the Prescribing Information. Not for patient distribution.

Pre-preparation: Gather the materials



The Beizray kit contains one or two single-use vials of docetaxel and a 50 mL vial of IV Solution Stabilizer made from 25% human albumin.

If previously refrigerated, allow vials to reach room temperature for approximately 5 minutes.

Preparation

Read this entire section carefully before mixing and diluting.

Inject 25% Albumin Human USP (IV Solution Stabilizer) directly into the 0.9% Sodium Chloride Injection bag.
Do not use 25% Albumin Human USP (IV Solution Stabilizer) to dilute Beizray.
To prevent precipitation, Beizray needs to be diluted with a prepared infusion bag containing Albumin Human USP and 0.9% Sodium Chloride Injection to ensure a final concentration between 0.14 mg/mL and 0.31 mg/mL. Follow the preparation instructions provided below.

1. Calculate the required amount of Beizray

Calculate the required amount of Beizray using the following formula:

- Required amount of Beizray (mL) = prescribed Beizray dose (mg/m^2) × body surface area (m^2) ÷ 20 (mg/mL)

2. Determine the required amount of 0.9% Sodium Chloride Injection

Based on the calculated amount of Beizray from Step 1, determine the required amount of 0.9% Sodium Chloride Injection:

Calculated amount of Beizray	Size of 0.9% Sodium Chloride Injection Infusion Bag
Beizray ≤ 8.8 mL	500 mL
Beizray > 8.8 mL	1,000 mL

3. Calculate the required amount of 25% Albumin Human USP (IV Solution Stabilizer)

Calculate the required amount of 25% Albumin Human USP (IV Solution Stabilizer) using the following formula:

Required amount of 25% Albumin Human USP (IV Solution Stabilizer) (mL) = Required amount of Beizray (mL) × 6

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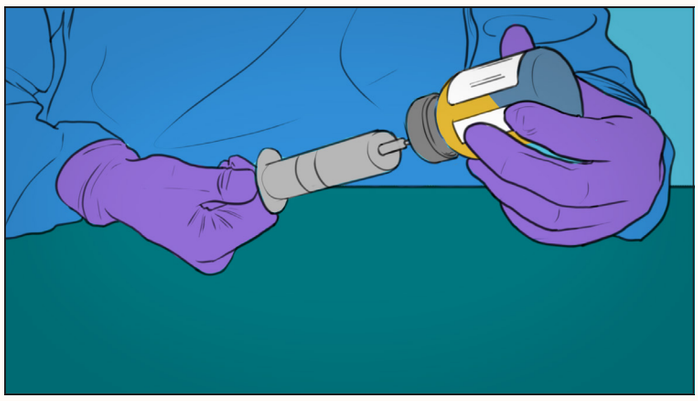
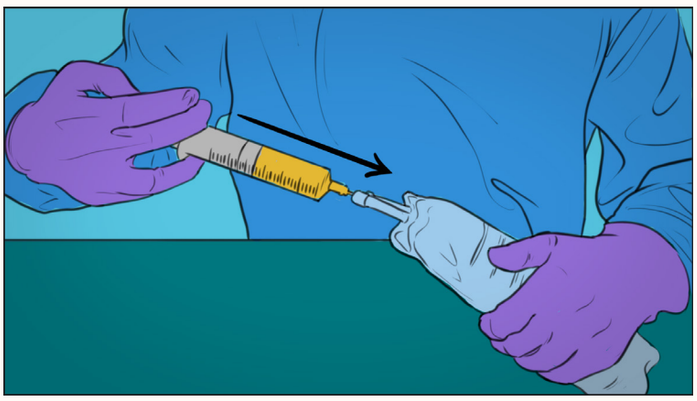
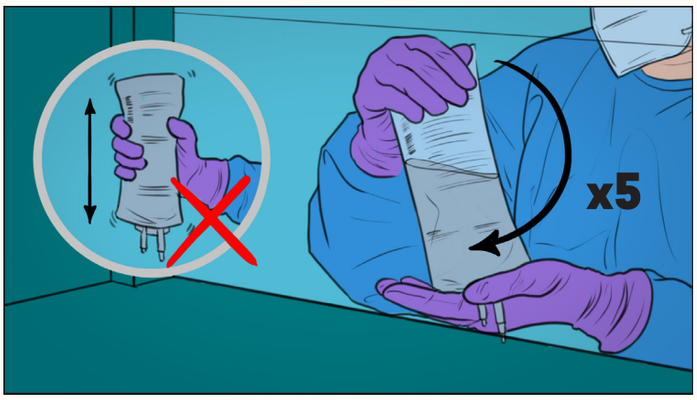
4. Add 25% Albumin Human USP (IV Solution Stabilizer) to the infusion bag



Withdraw the calculated amount of 25% Albumin Human USP (IV Solution Stabilizer) from the vial.



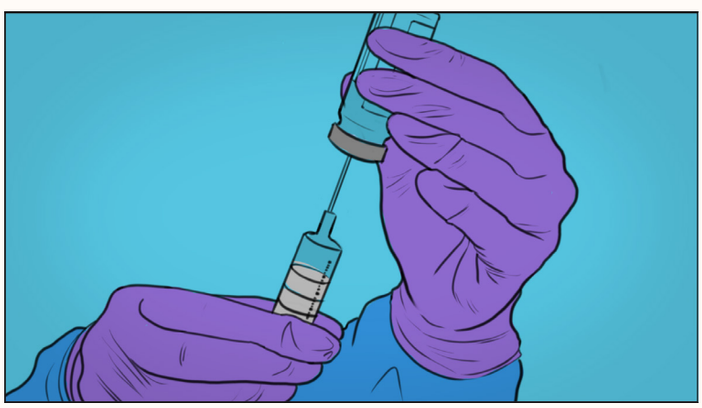
Inject into a 0.9% Sodium Chloride Injection bag.



Thoroughly mix the diluted solution by gently inverting the bag for at least 5 times. Do not shake.

This solution should be used immediately after preparation.

5. Add Beizray to the final solution



Aseptically withdraw the calculated amount of Beizray with a calibrated syringe.

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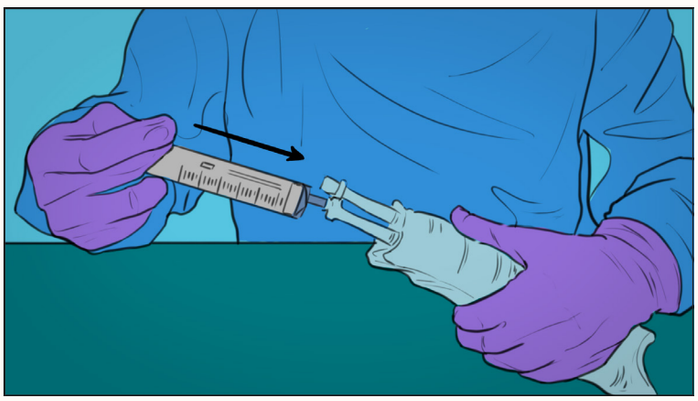
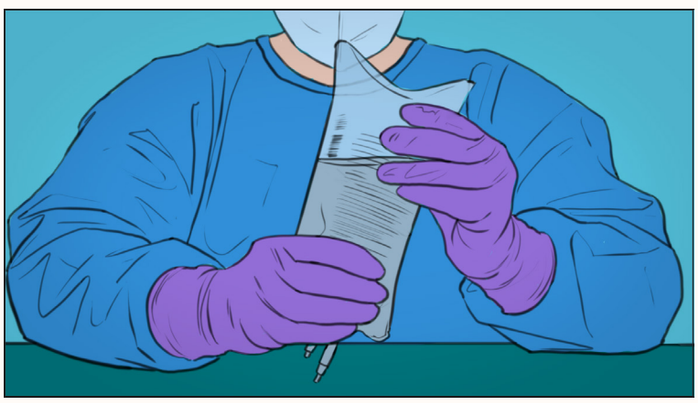


Inject via a single injection into the infusion bag containing the initial diluted solution with 25% Albumin Human USP (IV Solution Stabilizer) to produce a final concentration between 0.14 mg/mL and 0.31 mg/mL.

After injection, remove the syringe and immediately thoroughly mix the final infusion solution by gently inverting the bag for at least 10 times. Do not shake.

Discard any unused portion of Beizray vial(s) and 25% Albumin Human USP (IV Solution Stabilizer) vial(s).



Prior to administration, visually inspect Beizray final infusion solution for particulate matter or discoloration whenever the solution and container permit.

Discard the diluted Beizray infusion solution if the solution is not clear, discolored or appears to have precipitation, it should be discarded.

Beizray infusion solution is supersaturated, therefore may crystallize over time. If crystals appear, the solution must discarded.

The Beizray infusion solution should be administered intravenously as a **1-hour infusion** uunder ambient room temperature (below **25°C**) and lighting conditions

Beizray final infusion solution should be used immediately. However, if stored between **2°C** and **8°C (36°F and 46°F)**, infusion solution is stable for 24 hours.

If stored at **25°C (77°F)**, the final infusion solution is stable for **4 hours**. Beizray final infusion solution (in 0.9% Sodium Chloride Injection) should be used within 4 hours (including the 1 hour intravenous administration).

For further information on safety, handling, or dosing, always consult the full Prescribing Information.

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Important Safety Information

CONTRAINDICATION

BEIZRAY is contraindicated in patients with:

- neutrophil counts of <1500 cells/mm^3
- a history of severe hypersensitivity reactions to docetaxel. Severe reactions, including anaphylaxis, have occurred.

WARNINGS AND PRECAUTIONS

Toxic Deaths

Breast Cancer

BEIZRAY administered at 100 mg/m^2 was associated with deaths considered possibly or probably related to treatment in 2.0% (19/965) of metastatic breast cancer patients, both previously treated and untreated, with normal baseline liver function and in 11.5% (7/61) of patients with various tumor types who had abnormal baseline liver function (AST and/or ALT >1.5 times ULN together with AP >2.5 times ULN). Among patients dosed at 60 mg/m^2, mortality related to treatment occurred in 0.6% (3/481) of patients with normal liver function, and in 3 of 7 patients with abnormal liver function. Approximately half of these deaths occurred during the first cycle. Sepsis accounted for the majority of the deaths.

Non-small Cell Lung Cancer

BEIZRAY administered at a dose of 100 mg/m^2 in patients with locally advanced or metastatic non-small cell lung cancer who had a history of prior platinum-based chemotherapy was associated with increased treatment-related mortality (14% and 5% in two randomized, controlled studies). There were 2.8% treatment-related deaths among the 176 patients treated at the 75 mg/m^2 dose in the randomized trials. Among patients who experienced treatment-related mortality at the 75 mg/m^2 dose level, 3 of 5 patients had an ECOG PS of 2 at study entry.

Hepatic Impairment

Patients with elevations of bilirubin or abnormalities of transaminase concurrent with alkaline phosphatase are at increased risk for the development of severe neutropenia, febrile neutropenia, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity, and toxic death.

Avoid BEIZRAY in patients with bilirubin > upper limit of normal (ULN), or to patients with AST and/or ALT >1.5 x ULN concomitant with alkaline phosphatase >2.5 x ULN.

For patients with isolated elevations of transaminase >1.5 x ULN, consider BEIZRAY dose modifications. Measure bilirubin, AST or ALT, and alkaline phosphatase prior to each cycle of BEIZRAY therapy.

Hematologic Effects

Perform frequent peripheral blood cell counts on all patients receiving BEIZRAY. Do not retreat patients with subsequent cycles of BEIZRAY until neutrophils recover to a level >1500 cells/mm^3. Avoid retreating patients until platelets recover to a level >100,000 cells/mm^3.

A 25% reduction in the dose of BEIZRAY is recommended during subsequent cycles following severe neutropenia (<500 cells/mm^3) lasting 7 days or more, febrile neutropenia, or a grade 4 infection in a BEIZRAY cycle.

Neutropenia (<2000 neutrophils/mm^3) occurs in virtually all patients given 60 mg/m^2 to 100 mg/m^2 of BEIZRAY 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. Frequent monitoring of blood counts is, therefore, essential so that dose can be adjusted. BEIZRAY should not be administered to patients with neutrophils <1500 cells/mm^3.

Febrile neutropenia occurred in about 12% of patients given 100 mg/m^2 but was very uncommon in patients given 60 mg/m^2. Hematologic responses, febrile reactions and infections, and rates of septic death for different regimens are dose related.

Three breast cancer patients with severe liver impairment (bilirubin >1.7 times ULN) developed fatal gastrointestinal bleeding associated with severe drug-induced thrombocytopenia. In gastric cancer patients treated with docetaxel in combination with cisplatin and fluorouracil (TCF), febrile neutropenia and/or neutropenic infection occurred in 12% of patients receiving G-CSF compared to 28% who did not. Patients receiving TCF should be closely monitored during the first and subsequent cycles for febrile neutropenia and neutropenic infection.

Enterocolitis and Neutropenic Colitis

Enterocolitis and neutropenic colitis (typhlitis) have occurred in patients treated with BEIZRAY alone and in combination with other chemotherapeutic agents, despite the coadministration of G-CSF. Caution is recommended for patients with neutropenia, particularly at risk for developing gastrointestinal

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Important Safety Information (Cont)

Enterocolitis and Neutropenic Colitis (Cont)
complications. Enterocolitis and neutropenic enterocolitis may develop at any time, and could lead to death as early as the first day of symptom onset. Monitor patients closely from onset of any symptoms of gastrointestinal toxicity. Inform patients to contact their healthcare provider with new, or worsening symptoms of gastrointestinal toxicity.

Hypersensitivity Reactions
Monitor patients closely for hypersensitivity reactions, especially during the first and second infusions. Severe hypersensitivity reactions characterized by generalized rash/erythema, hypotension and/or bronchospasm, or fatal anaphylaxis, have been reported in patients premedicated with 3 days of corticosteroids. Severe hypersensitivity reactions require immediate discontinuation of the BEIZRAY infusion and aggressive therapy. Do not rechallenge patients with a history of severe hypersensitivity reactions with BEIZRAY. Patients who have previously experienced a hypersensitivity reaction to paclitaxel may develop a hypersensitivity reaction to docetaxel that may include severe or fatal reactions such as anaphylaxis. Monitor patients with a previous history of hypersensitivity to paclitaxel closely during initiation of BEIZRAY therapy. Hypersensitivity reactions may occur within a few minutes following initiation of a BEIZRAY infusion. If minor reactions such as flushing or localized skin reactions occur, interruption of therapy is not required. All patients should be premedicated with an oral corticosteroid prior to the initiation of the infusion of BEIZRAY.

Fluid Retention
Severe fluid retention has been reported following BEIZRAY therapy. Patients should be premedicated with oral corticosteroids prior to each BEIZRAY administration to reduce the incidence and severity of fluid retention. Patients with pre-existing effusions should be closely monitored from the first dose for the possible exacerbation of the effusions. When fluid retention occurs, peripheral edema usually starts in the lower extremities and may become generalized with a median weight gain of 2 kg.
Among 92 breast cancer patients premedicated with 3-day corticosteroids, moderate fluid retention occurred in 27.2% and severe fluid retention in 6.5%. The median cumulative dose to onset of moderate or severe fluid retention was 819 mg/m^2. Nine of 92 patients (9.8%) of patients discontinued treatment due to fluid retention: 4 patients discontinued with severe fluid retention; the remaining 5 had mild or moderate fluid retention. The median cumulative dose to treatment discontinuation due to fluid retention was 1021 mg/m^2. Fluid retention was completely, but sometimes slowly, reversible with a median of 16 weeks from the last infusion of BEIZRAY to resolution (range: 0 to 42+ weeks). Patients developing peripheral edema may be treated with standard measures, e.g., salt restriction, oral diuretic(s).

Second Primary Malignancies
Second primary malignancies, notably acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), non Hodgkin's lymphoma (NHL), and renal cancer, have been reported in patients treated with docetaxel-containing regimens. These adverse reactions may occur several months or years after docetaxel-containing therapy. Treatment-related AML or MDS has occurred in patients given anthracyclines and/or cyclophosphamide, including use in adjuvant therapy for breast cancer. In the adjuvant breast cancer trial (TAX316) AML occurred in 3 of 744 patients who received BEIZRAY, doxorubicin and cyclophosphamide (TAC) and in 1 of 736 patients who received fluorouracil, doxorubicin, and cyclophosphamide. In TAC-treated patients, the risk of delayed myelodysplasia or myeloid leukemia requires hematological follow-up. Monitor patients for second primary malignancies.

Cutaneous Reactions
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. The discontinuation rate due to skin toxicity was 1.6% (15/965) for metastatic breast cancer patients. Among 92 breast cancer patients premedicated with 3-day corticosteroids, there were no cases of severe skin toxicity reported and no patient discontinued BEIZRAY due to skin toxicity.
Severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with docetaxel treatment. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. Permanent treatment discontinuation should be considered in patients who experience SCARs.

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Neurologic Reactions
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. Patients who experienced neurotoxicity in clinical trials and for whom follow-up information on the complete resolution of the event was available had spontaneous reversal of symptoms with a median of 9 weeks from onset (range: 0 to 106 weeks). Severe peripheral motor neuropathy mainly manifested as distal extremity weakness occurred in 4.4% (42/965).

Eye Disorders
Cystoid macular edema (CME) has been reported in patients treated with docetaxel. Patients with impaired vision should undergo a prompt and comprehensive ophthalmologic examination. If CME is diagnosed, BEIZRAY treatment should be discontinued and appropriate treatment initiated. Alternative non-taxane cancer treatment should be considered.

Asthenia
Severe asthenia has been reported in 14.9% (144/965) of metastatic breast cancer patients but has 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.

Embryo-Fetal Toxicity
Based on findings from animal reproduction studies and its mechanism of action, BEIZRAY can cause fetal harm when administered to a pregnant woman. Available data from case reports in the literature and pharmacovigilance with docetaxel use in pregnant women are not sufficient to inform the drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies, administration of docetaxel to pregnant rats and rabbits during the period of organogenesis caused embryo-fetal toxicities, including intrauterine mortality, at doses as low as 0.02 and 0.003 times the recommended human dose based on body surface area, respectively.

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify pregnancy status in females of reproductive potential prior to initiating BEIZRAY. Advise females of reproductive potential to use effective contraception during treatment and for 2 months after the last dose of BEIZRAY. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of BEIZRAY.

Alcohol Content
Cases of intoxication have been reported with some formulations of docetaxel due to the alcohol content. The alcohol content in a dose of BEIZRAY may affect the central nervous system and should be taken into account for patients in whom alcohol intake should be avoided or minimized. Consideration should be given to the alcohol content in BEIZRAY on the ability to drive or use machines immediately after the infusion. Each administration of BEIZRAY Injection at 100 mg/m^2 delivers 4.0 g/m^2 of ethanol. For a patient with a BSA of 2.0 m^2, this would deliver 8.0 grams of ethanol. Other docetaxel products may have a different amount of alcohol.

Tumor Lysis Syndrome
Tumor lysis syndrome has been reported with docetaxel. Patients at risk of tumor lysis syndrome (e.g., with renal impairment, hyperuricemia, bulky tumor) should be closely monitored prior to initiating BEIZRAY and periodically during treatment. Correction of dehydration and treatment of high uric acid levels are recommended prior to initiation of treatment.

Transmissible Infectious Agents
BEIZRAY final infusion solution contains human albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries a remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob Disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

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ADVERSE REACTIONS

The most serious adverse reactions from BEIZRAY are Toxic Deaths, Hepatic Impairment, Hematologic Effects, Enterocolitis and Neutropenic Colitis, Hypersensitivity Reactions, Fluid Retention, Second Primary Malignancies, Cutaneous Reactions, Neurologic Reactions, Eye Disorders, Asthenia, Alcohol Content, Tumor Lysis Syndrome.

The most common adverse reactions across all docetaxel 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. Incidence varies depending on the indication.

Clinical Trials Experience

Adverse events occurring in at least 5% of patients with various tumor types
Adverse reactions occurring in breast cancer patients, both treated and untreated with chemotherapy, with normal liver function tests at baseline who were treated with docetaxel 100 mg/m^2 and those occurring in patients with various tumor types who had normal or elevated liver function tests at baseline who were treated with docetaxel 100 mg/m^2 were neutropenia <2000 cells/mm^3 (96% all tumor types with normal liver function tests, 96% all tumor types with elevated liver function tests, 99% breast cancer with normal liver function tests, respectively), neutropenia <500 cells/mm^3 (75%, 88%, 86%, respectively), leukopenia <4000 cells/mm^3 (96%, 98%, 99%, respectively), leukopenia <1000 cells/mm^3 (32%, 47%, 44%, respectively), thrombocytopenia <100,000 cells/mm^3 (8%, 25%, 9%, respectively), anemia <11 g/dL (90%, 92%, 94%, respectively), anemia <8 g/dL (9%, 31%, 8%, respectively), severe febrile neutropenia (11%, 26%, 12%, respectively), infections (severe; 6%, 16%, 6%, respectively), infections (any; 22%, 33%, 22%, respectively), fever in the absence of infection (severe; 2%, 8%, 2%, respectively), fever in the absence of infection (any; 31%, 41%, 35%, respectively), hypersensitivity reactions regardless of premedication (severe; 4%, 10%, 3%, respectively), hypersensitivity reactions regardless of premedication (any; 21%, 20%,,8%, respectively), hypersensitivity reactions with 3-day premedication (severe; 2%, 0%, 2%, respectively), hypersensitivity reactions with 3-day premedication (any; 15%, 33%, 15%, respectively), fluid retention regardless of premedication (severe; 7%, 8%, 9%, respectively), fluid retention regardless of premedication (any; 47%, 39%, 60%, respectively, fluid retention with 3-day premedication (severe; 7%, 33%, 7%, respectively), fluid retention with 3-day premedication (any; 64%, 67%, 64%, respectively), neurosensory (severe; 4%, 0%, 6%, respectively), neurosensory (any; 49%, 34%, 58%, respectively), cutaneous (severe; 5%, 10%, 5%, respectively), cutaneous (any; 48%, 54%, 47%, respectively), nail changes (severe; 3%, 5%, 4%, respectively), nail changes (any; 31%, 23%, 41%, respectively), gastrointestinal (severe; 5%, 5%, 6%, respectively), nausea (39%, 38%, 42%, respectively), vomiting (22%, 23%, 23%, respectively), diarrhea (39%, 33%, 43%, respectively), stomatitis (severe; 6%, 13%, 7%, respectively), stomatitis (any; 42%, 49%, 52%, respectively), alopecia (76%, 62%, 74%, respectively), asthenia (severe; 13%, 25%, 15%, respectively), asthenia (any; 62%, 53%, 66%, respectively), myalgia (severe; 2%, 2%, 2%, respectively), myalgia (any; 19%, 16%, 21%, respectively), arthralgia (9%, 7%, 8%, respectively), and infusion site reactions (4%, 3%, 4%, respectively). Septic death (2%, 5%, 1%, respectively) and non-septic death (1%, 7%, 1%, respectively) also occurred.

Monotherapy with docetaxel for locally advanced or metastatic breast cancer after failure of prior chemotherapy
Hematologic adverse reactions (Grade 3/4) occurring in breast cancer patients previously treated with chemotherapy with normal or elevated liver function tests who were treated with docetaxel 100 mg/m^2 or those with normal liver function tests who were treated with docetaxel 60 mg/m^2 were neutropenia <500 cells/mm^3 (84%, 94%, and 75% at 100 mg/m^2 with normal liver function tests, 100 mg/m^2 with elevated liver function test, and at 60 mg/m^2 with normal liver function tests, respectively), thrombocytopenia <20,000 cells/mm^3 (1%,17%,1%, respectively), infection (7%,33%,0%, respectively), febrile neutropenia by patient (12%,33%,0%, respectively), and febrile neutropenia by course (2%,9%,0%, respectively).

Severe non-hematologic adverse reactions occurring in breast cancer patients previously treated with chemotherapy with normal or elevated liver function tests who were treated with docetaxel 100 mg/m^2 or those with normal liver function tests who were treated with docetaxel 60 mg/m^2 were acute hypersensitivity reaction regardless of premedication (1%,0%, and 0% at 100 mg/m^2 with normal liver function tests, 100 mg/m^2

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with elevated liver function test, and at 60 mg/m^2 with normal liver function tests, respectively), fluid retention regardless of premedication (8%,17%,0%, respectively), neurosensory (6%,0%,0%, respectively), cutaneous (5%,17%,0%, respectively), asthenia (17%,22%,0%, respectively), diarrhea (6%,11%, NA, respectively), and stomatitis (8%, 39%, 1%, respectively).

Septic death (2%,6%,1%, respectively), and non-septic death (1%,11%,0%, respectively) also occurred.

Monotherapy trial (TAX313) comparing docetaxel 60 mg/m^2, 75 mg/m^2 and 100 mg/m^2 in advanced breast cancer
The following adverse reactions were associated with increasing docetaxel doses: fluid retention (26%, 38%, and 46% at 60 mg/m^2, 75 mg/m^2, and 100 mg/m^2, respectively), thrombocytopenia (7%,11%,12%, respectively), neutropenia (92%, 94%, 97% respectively), febrile neutropenia (5%,7%,14%, respectively), treatment-related grade 3 or 4 infection (2%, 3%, 7%, respectively) and anemia (87%, 94%, 97%, respectively).
Combination therapy with Docetaxel in the adjuvant treatment of breast cancer
Adverse reactions (Grade 3/4) occurring in patients with breast cancer who were treated with Docetaxel 75 mg/m^2 every 3 weeks in combination with doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 (TAX316) were anemia (4%), neutropenia (66%), fever in the absence of infection (1%), infection (4%), thrombocytopenia (2%), hypersensitivity reactions (1%), fluid retention (1%), neuro-cortical (1%), syncope (1%), skin toxicity (1%), nausea (5%), stomatitis (7%), vomiting (4%), diarrhea (4%), constipation (1%), taste perversion (1%), anorexia (2%), abdominal pain (1%), vasodilation (1%), asthenia (11%), myalgia (1%), and arthralgia (1%).

Monotherapy with docetaxel for unresectable, locally advanced or metastatic non-small cell lung cancer (NSCLC) previously treated with platinum-based chemotherapy
Adverse reactions (Grade 3/4 or severe) occurring in patients with locally advanced or metastatic NSCLC and a history of prior treatment with platinum-based chemotherapy who were treated with docetaxel 75 mg/m^2 monotherapy were neutropenia (65%), leukopenia (49%), thrombocytopenia (3%), anemia (9%), febrile neutropenia (6%), infection (10%), hypersensitivity reactions (3%), fluid retention (3%), neurosensory (2%), neuromotor (5%), skin (1%), nausea (5%), vomiting (3%), diarrhea (3%), asthenia (18%), stomatitis (2%), pulmonary (21%), nail disorder (1%), taste perversion (1%), and treatment related mortality (3%).

Combination therapy with docetaxel in chemotherapy-naïve advanced unresectable or metastatic NSCLC
Adverse reactions (Grade 3/4 or severe) occurring in patients with unresectable stage IIIB or IV NSCLC and no history of prior chemotherapy who were treated with docetaxel 75 mg/m^2 in combination with cisplatin 75 mg/m^2 (TAX326) were neutropenia (74%), thrombocytopenia (3%), anemia (7%), infection (8%), fever in the absence of infection (<1%), hypersensitivity reaction (3%), fluid retention (2%), pleural effusion (2%), peripheral edema (<1%), weight gain (<1%), neurosensory (4%), neuromotor (3%), skin (<1%), nausea (10%), vomiting (8%), diarrhea (7%), anorexia (5%), stomatitis (2%), alopecia (<1%), asthenia (12%), nail disorders (<1%), and myalgia (<1%).

Combination therapy with docetaxel in patients with castration-resistant prostate cancer (CRPC)
Adverse reactions (Grade 3/4) occurring in patients with CRPC who were treated with docetaxel 75 mg/m^2 every 3 weeks in combination with prednisone 5 mg orally twice daily (TZX327) were anemia (5%), neutropenia (32%), thrombocytopenia (1%), infection (6%), allergic reactions (1%), fluid retention (1%), neuropathy sensory (2%), neuropathy motor (2%), nausea (3%), diarrhea (2%), stomatitis/pharyngitis (1%), vomiting (2%), anorexia (1%), dyspnea (3%), fatigue (5%), tearing (1%), and arthralgia (1%).

Combination therapy with docetaxel in gastric adenocarcinoma
Adverse reactions (Grade 3/4) occurring in patients with advanced gastric adenocarcinoma and no history of prior chemotherapy for advanced disease who were treated with docetaxel 75 mg/m^2 in combination with cisplatin 75 mg/m^2 and fluorouracil 750 mg/m^2 include anemia (18%), neutropenia (82%), fever in the absence of infection (2%), thrombocytopenia (8%), infection (16%), allergic reactions (2%), lethargy (21%), neurosensory (8%), neuromotor (3%), dizziness (5%), alopecia (5%), rash/itch (1%), nausea (16%), vomiting (15%), anorexia (13%), stomatitis (21%), diarrhea (20%), constipation (2%), esophagitis/dysphagia/odynophagia (2%), gastrointestinal pain/cramping (2%), and cardiac dysrhythmias (2%).

Combination therapy with docetaxel in head and neck cancer
Adverse reactions (Grade 3/4) occurring in patients with squamous cell carcinoma of the head and neck (SCCHN) who received induction chemotherapy with docetaxel 75 mg/m^2 in combination with cisplatin

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Important Safety Information (Cont)

75 mg/m^2 and fluorouracil 750 mg/m^2 followed by radiotherapy (TAX323) or chemoradiotherapy (TAX 324), were neutropenia (76%, 84% with combination therapy followed by radiotherapy [TAX323] or chemoradiotherapy [TAX324], respectively), anemia (9%,12%, respectively), thrombocytopenia (5%, 4%, respectively), infection (9%,6%, respectively), cancer pain (5%,9%, respectively), lethargy (3%,5%, respectively), fever in the absence of infection (1%,4%, respectively), myalgia (1%,0%, respectively), weight loss (1%,2%, respectively), fluid retention (0%,1%, respectively), edema (0%,1%, respectively), dizziness (0%,4%, respectively), neurosensory (1%,1%, respectively), altered hearing (0%,1%, respectively), neuromotor (1%,0%, respectively), alopecia (11%,4%, respectively), desquamation (1%,0%, respectively), nausea (1%,14%, respectively), stomatitis (4%,21%, respectively), vomiting (1%,8%, respectively), diarrhea (3%,7%, respectively), constipation (1%,1%, respectively), anorexia (1%,12%, respectively), esophagitis/dysphagia/odynophagia (1%,13%, respectively), gastrointestinal pain/cramping (1%,5%, respectively), heartburn (0%,2%, respectively), gastrointestinal bleeding (2%,1%, respectively), cardiac dysrhythmia (2%,3%, respectively), venous (2%,2%, respectively), and ischemia myocardial (2%,1%, respectively).

USE IN SPECIFIC POPULATIONS

Pregnancy
Based on findings in animal studies and its mechanism of action, BEIZRAY can cause fetal harm when administered to a pregnant woman. Available data from case reports in the literature and pharmacovigilance with docetaxel use in pregnant women are not sufficient to inform the drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. BEIZRAY contains alcohol which can interfere with neurobehavioral development.

Lactation
There is no information regarding the presence of docetaxel in human milk, or on its effects on milk production or the breastfed child. Advise women not to breastfeed during treatment with BEIZRAY and for 1 week after the last dose. BEIZRAY contains alcohol which can interfere with neurobehavioral development. Advise women not to breastfeed during treatment with BEIZRAY and for 1 week after the last dose. BEIZRAY contains alcohol which can interfere with neurobehavioral development.

Females and Males of Reproductive Potential
Verify pregnancy status in females of reproductive potential prior to initiating BEIZRAY. Advise females of reproductive potential to use effective contraception during treatment and for 2 months after the last dose of BEIZRAY. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of BEIZRAY. Based on findings in animal studies, BEIZRAY may impair fertility in males of reproductive potential.

Pediatric Use
The alcohol content of BEIZRAY should be taken into account when given to pediatric patients. The efficacy of BEIZRAY in pediatric patients as monotherapy or in combination has not been established. The overall safety profile of BEIZRAY in pediatric patients receiving monotherapy or TCF was consistent with the known safety profile in adults.

Geriatric Use
Dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy in elderly patients.

Non-small Cell Lung Cancer
Patients ≥65 years of age with non-small cell lung cancer treated with docetaxel+cisplatin were more likely to experience diarrhea (55%), infections (42%), peripheral edema (39%) and stomatitis (28%) compared to patients less than the age of 65 administered the same treatment (43%, 31%, 31% and 21%, respectively). In patients ≥ 65 years of age treated with docetaxel+cisplatin, diarrhea (55%), peripheral edema (39%) and stomatitis (28%) were observed more frequently than in the vinorelbine+cisplatin group (diarrhea 24%, peripheral edema 20%, stomatitis 20%). When docetaxel was combined with carboplatin for the treatment of chemotherapy-naive, advanced non-small cell lung carcinoma, patients ≥65 years (28%) experienced higher frequency of infection compared to similar patients treated with docetaxel+cisplatin, and a higher frequency of diarrhea,

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Important Safety Information (Cont)

infection and peripheral edema than elderly patients treated with vinorelbine+cisplatin.

Prostate Cancer
In patients ≥65 years of age with prostate cancer treated with docetaxel every three weeks plus prednisone, the following treatment-emergent adverse reactions occurred at rates ≥10% higher compared to younger patients: anemia (71% vs 59%), infection (37% vs 24%), nail changes (34% vs 23%), anorexia (21% vs 10%), weight loss (15% vs 5%), respectively.

Breast Cancer
In the adjuvant breast cancer trial (TAX316), docetaxel in combination with doxorubicin and cyclophosphamide was administered to 744 patients of whom 48 (6%) were 65 years of age or greater. The number of elderly patients who received this regimen was not sufficient to determine whether there were differences in safety and efficacy between elderly and younger patients.

Gastric Cancer
The number of patients ≥65 years of age with gastric cancer treated with docetaxel in combination with cisplatin and fluorouracil was not sufficient to determine whether they respond differently from younger patients. However, the incidence of serious adverse reactions was higher in patients ≥65 years of age compared to younger patients. The incidence of the following adverse reactions (all grades, regardless of relationship): lethargy, stomatitis, diarrhea, dizziness, edema, febrile neutropenia/neutropenic infection occurred at rates ≥10% higher in patients who were 65 years of age or older compared to younger patients. Elderly patients treated with TCF should be closely monitored.

Hepatic Impairment
Avoid BEIZRAY in patients with bilirubin >ULN and patients with AST and/or ALT >1.5 × ULN concomitant with alkaline phosphatase >2.5 × ULN. The alcohol content of BEIZRAY should be taken into account when given to patients with hepatic impairment.

Please see accompanying full Prescribing Information, including Boxed Warning, also available at the QR code

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