DOCIVYX™
(docetaxel) injection

Billing and Coding Guide

If you have additional billing and coding questions, please call your Field Reimbursement Manager or AVYXASSIST™ at 866-939-8927. Our Patient Access Specialists are available to assist Monday through Friday, 8 AM to 8 PM ET.

Please see Important Safety Information on pages 3, 4 and 14-21 and full Prescribing Information for DOCIVYX including BOXED WARNING.

AVYXA

Table of Contents

The contents herein provide general coverage, coding, and payment information about DOCIVYX™. The information within this guide was obtained from third-party sources and is made available for reference only. It is not exhaustive, is subject to change, and does not constitute billing, coding, or legal advice. Healthcare professionals are responsible for determining which code(s), charge(s), or modifier(s), if any, appropriately reflect a service or diagnosis. It is the healthcare professional's responsibility to determine medical necessity and provide adequate documentation. AVYXA™ does not guarantee coverage or payment. Payment and coverage vary by payer. Questions about coding, coverage, and payment may be directed to the applicable third-party payer, reimbursement specialist, and/or legal counsel.

CMS: Centers for Medicare & Medicaid Services; CPT: Current Procedural Terminology; HCPCS: Healthcare Common Procedure Coding System; ICD: International Classification of Diseases; NDC: National Drug Code

Please see Important Safety Information on pages 3, 4 and 14-21 and full Prescribing Information for DOCIVYX including BOXED WARNING.

INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

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

Treatment-related mortality associated with DOCIVYX 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 DOCIVYX as a single agent at a dose of 100 mg/m^2.

Avoid the use of DOCIVYX 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. 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. Patients with isolated elevations of transaminase >1.5 x ULN also had a higher rate of febrile neutropenia. Measure bilirubin, AST or ALT, and alkaline phosphatase prior to each cycle of DOCIVYX.

Do not administer DOCIVYX to patients with neutrophil counts of <1500 cells/mm^3. Monitor blood counts frequently as neutropenia may be severe and result in infection.

Do not administer DOCIVYX to patients who have a history of severe hypersensitivity reactions to DOCIVYX. Severe hypersensitivity reactions have been reported in patients despite dexamethasone premedication. Hypersensitivity reactions require immediate discontinuation of the DOCIVYX infusion and administration of appropriate therapy.

Severe fluid retention occurred in 6.5% (6/92) of patients despite use of dexamethasone premedication. 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).

INDICATIONS AND USAGE

Breast Cancer

- DOCIVYX is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.
- DOCIVYX in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.

Non-small Cell Lung Cancer

- DOCIVYX 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.
- DOCIVYX 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.

Prostate Cancer

- DOCIVYX in combination with prednisone is indicated for the treatment of patients with metastatic CRPC.

Gastric Adenocarcinoma

- DOCIVYX 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.

Head and Neck Cancer

- DOCIVYX 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 (SCCHN).

DOCIVYX™
(docetaxel) injection

DOCIVYX™ Ordering Information

To order DOCIVYX™ (docetaxel) injection, please contact one of these authorized specialty distributors and use the appropriate order #:

20 mg/2 mL (10 mg/mL)
NDC: 83831-101-02

80 mg/8 mL (10 mg/mL)
NDC: 83831-102-08

160 mg/16 mL (10 mg/mL)
NDC: 83831-103-16

Institutions/Hospitals			
Cardinal Health Specialty	5918164	5918172	5918180
CENCORA - ASD Healthcare	10288612	10288614	10288615
McKesson Plasma & Biologics	2933505	2933521	2933539
Physician Offices			
Cardinal Health Specialty	5918164	5918172	5918180
Oncology Supply	10288544	10288613	10288545
McKesson Specialty Health	5017502	5017503	5017504

Supplied as a Solution

- Polysorbate-80 free formulation
- No reconstitution required
- Supplied as a solution in a single-dose vial ready to add to the infusion solution
- Ready to add to the infusion solution with two different options; 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP
- Store unopened vials between 2°C and 25°C (36°F and and 77°F)

INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (CONTINUED)

CONTRAINDICATION

DOCIVYX™ 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.

Please see Important Safety Information on pages 3, 4 and 14-21 and full Prescribing Information for DOCIVYX including BOXED WARNING.

AVYXASSIST™

Simplifying Patient Access, Providing Comprehensive Support.

AVYXASSIST™ can offer support to qualifying patients in need. The program provides the following services*

- Benefit verification
- Prior authorization requirements
- Appeals process information
- Referrals to 501(c)(3) foundations when applicable
- Free product assistance (uninsured or underinsured), bridge supply (coverage delays)
- Product replacement
- Copay assistance

DOCIVYX™ COPAY ASSISTANCE

Patients prescribed DOCIVYX™ may pay as little as **$0** per dose*

TO ENROLL, PLEASE CHOOSE ONE OF THE FOLLOWING OPTIONS

Phone

866-939-8927
Monday through Friday
8 AM to 8 PM ET

CALL NOW

OR

Online

Click on the link below to begin your online enrollment

ENROLL NOW

OR

Fax

Download, print and fax the completed enrollment form to 833-852-3420

DOWNLOAD NOW

*For eligibility requirements please contact a Patient Access Specialist. Terms and conditions apply.

DOCIVYX™
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Billing and Coding Information

The information provided is for informational purposes only and represents no statement, promise, or guarantee by AVYXA™ concerning reimbursement, payment, or charges. The information provided is not intended to increase or maximize reimbursement by any payer. Healthcare professionals are responsible for selecting appropriate codes used to file a claim. Codes should be based on the patient's diagnosis and the items and services furnished by the healthcare professional. All codes should be verified between the healthcare professional and payer. AVYXA™ does not recommend the use of any particular diagnosis code in any billing situation for DOCIVYX™. The below codes are for reference only; coding as submitted is the sole responsibility of the prescribing physician.

NDCs for DOCIVYX™[1]

NDC	Vial Size
83831-0101-02	Carton of 1 single-dose vial, 20 mg/2 mL (10 mg/mL)
83831-0102-08	Carton of 1 single-dose vial, 80 mg/8 mL (10 mg/mL)
83831-0103-16	Carton of 1 single-dose vial, 160 mg/16 mL (10 mg/mL)

HCPCS Code[2]

HCPCS Level II codes[3] are used to identify most drugs and biologics that are given in the office.

DOCIVYX™ Unique J-Code	Description
J9172	Injection, docetaxel not therapeutically equivalent to J9171, 1 mg

J-Code Billing Unit Conversion

Each 1 mg of DOCIVYX™ is equivalent to one (1) billing unit. When billing for quantities greater than 1 mg, indicate the total amount used as a multiple of billing units on the claim form. Examples:

One (1) Vial (2 ml) or 20 mg	20 billing units
One (1) Vial (8 ml) or 80 mg	80 billing units
One (1) Vial (16 ml) or 160 mg	160 billing units

NOTE: There are a few HCPCS codes for docetaxel so please make sure the HCPCS code matches the product purchased and administered.

HCPCS: Healthcare Common Procedure Coding System; NDC: National Drug Code

Please see Important Safety Information on pages 3, 4 and 14-21 and full Prescribing Information for DOCIVYX including BOXED WARNING.

CPT Drug Administration Codes[4]

CPT codes are used to bill for drug administration services provided in both the physician's office and other outpatient settings. DOCIVYX™ has a one-hour infusion time for differing indications. However, please code according to start and stop times listed in the patient's medical chart.

CPT Code	CPT Code Descriptor
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96417	Chemotherapy administration, intravenous infusion technique; each additional sequential infusion (different substance/drug), up to 1 hour

ICD Diagnosis Codes

International Classification of Disease, 10th Edition, Clinical Modification Codes for DOCIVYX™	
Indication	**ICD-10 Codes[5]**
Breast Cancer	C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321, C50.322, C50.329,C50.411, C50.412, C50.419, C50.421, C50.422, C50.429, C50.511, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929
Encounter for Chemotherapy[6]*	Z51.11
Gastric Cancer	C16.0, C16.1, C16.2, C16.3, C16.4, C16.5, C16.6, C16.8, C16.9
Head and Neck Cancer	C00.0, C00.1, C00.2, C00.3, C00.4, C00.5, C00.6, C00.8, C00.9, C01, C02.0, C02.1, C02.2, C02.3, C02.4, C02.8, C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.9, C05.0, C05.1, C05.2, C05.8, C05.9, C06.0, C06.1, C06.80, C06.89, C06.9, C09.0, C07, C08.0, C08.9, C09.1, C09.8, C09.9, C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C11.0, C11.1, C11.2, C11.3, C11.8, C11.9, C12, C13.0, C13.1, C13.2, C13.8, C13.9, C14.2, C14.8, C32.0, C32.1, C32.2, C32.3, C32.8, C32.9, C76.0
Non-Small Cell Lung Cancer	C33, C34.00, C34.01, C34.02, C34.10, C34.11, C34.12, C34.30, C34.31, C34.32, C34.80, C34.81, C34.82, C34.90, C34.91, C34.92
Prostate Cancer	C61

Please refer to the individual payer policy for a list of specific coverage criteria. ICD-10-CM diagnosis code must be clearly and explicitly noted in the patient medical record.

*For drugs with multiple indications, it is best practice to code the most specific ICD-10-CM code within the indication, to justify medical necessity.

AMA: American Medical Association; CMS: Centers for Medicare & Medicaid Services; CPT: Current Procedural Terminology; FARS: Federal Acquisition Regulation Supplement; HHSARS: Health and Human Services Acquisition Regulation; ICD: International Classification of Diseases NDC: National Drug Codes

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DOCIVYX™ Billing and Coding Information: ICD Diagnosis Codes by Indication[5]

ICD-10-CM coding for DOCIVYX™ varies greatly by payer. This coding is one alternative that adheres to ICD-10-CM Guidelines. Please check with each payer to ascertain the best coding for DOCIVYX™ according to their policy.

Breast Cancer: ICD-10-CM Diagnosis Coding	
ICD-10 Code	**Descriptor**
C50.011 - C50.019	Malignant neoplasm of nipple and areola, female
C50.021 - C50.029	Malignant neoplasm of nipple and areola, male
C50.111 - C50.119	Malignant neoplasm of nipple and areola, female
C50.121 - C50.129	Malignant neoplasm of central portion of breast, male
C50.211 - C50.219	Malignant neoplasm of upper-inner quadrant of breast, female
C50.221 - C50.229	Malignant neoplasm of upper-inner quadrant of breast, male
C50.311 - C50.319	Malignant neoplasm of lower-inner quadrant of breast, female
C50.321 - C50.329	Malignant neoplasm of lower-inner quadrant of breast, male
C50.411 - C50.419	Malignant neoplasm of upper-outer quadrant of breast, female
C50.421 - C50.429	Malignant neoplasm of upper-outer quadrant of breast, male
C50.511 - C50.519	Malignant neoplasm of lower-outer quadrant of breast, female
C50.521 - C50.529	Malignant neoplasm of lower-outer quadrant of breast, male
C50.611 - C50.619	Malignant neoplasm of axillary tail of breast, female
C50.621 - C50.629	Malignant neoplasm of axillary tail of breast, male
C50.811 - C50.819	Malignant neoplasm of overlapping sites of breast, female
C50.821 - C50.829	Malignant neoplasm of overlapping sites of breast, male
C50.911 - C50.919	Malignant neoplasm of breast of unspecified site, female
C50.921 - C50.929	Malignant neoplasm of breast of unspecified site, male

Gastric Cancer: ICD-10-CM Diagnosis Coding	
ICD-10 Code	**Descriptor**
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified

Head and Neck Cancer: ICD-10-CM Diagnosis Coding	
ICD-10 Code	**Descriptor**
C00.0 - C00.9	Malignant neoplasm of lip
C01	Malignant neoplasm of base of tongue
C02.0 - C02.9	Malignant neoplasm of other and unspecified parts of tongue
C03.0 - C03.9	Malignant neoplasm of gum
C04.0 - C04.9	Malignant neoplasm of floor of mouth
C05.0 - C05.9	Malignant neoplasm of palate
C06.0 - C06.9	Malignant neoplasm of other and unspecified parts of the mouth
C07	Malignant neoplasm of parotid gland
C08.0 - C08.9	Malignant neoplasm of other and unspecified major salivary glands
C09.0 - C09.9	Malignant neoplasm of tonsil
C10.0 - C10.9	Malignant neoplasm of oropharynx
C11.0 - C11.9	Malignant neoplasm of nasopharynx
C12	Malignant neoplasm of pyriform sinus
C13.0 - C13.9	Malignant neoplasm of hypopharynx
C14.0 - C14.8	Malignant neoplasm of other and ill-defined sites in the lip, oral cavity, and pharynx
C32.0 - C32.9	Malignant neoplasm of larynx
C76.0	Malignant neoplasm of head, face, and neck

Lung Cancer: ICD-10-CM Diagnosis Coding	
ICD-10 Code	**Descriptor**
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of right bronchus or lung

Prostate Cancer: ICD-10-CM Diagnosis Coding	
ICD-10 Code	**Descriptor**
C61	Malignant neoplasm of prostate

ICD: International Classification of Diseases

Sample Claim Form CMS-1450 (UB-04)[7]

This information is provided for educational purposes only and is not a guarantee of coverage. It is the sole responsibility of the healthcare professional to select the proper codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

Form Locator (FL) 42 (Electronic Claim Form = Loop 2400, Segment Type SV201):
List the appropriate revenue code for the drug. Match the descriptor for DOCIVYX™ to your revenue code, 0636.
Additionally, enter an appropriate revenue code for the administration service, 0335 for chemotherapy, or others based on the cost center in which the service was performed.

FL 42

FL 43 (NOT REQUIRED BY MEDICARE):
Enter the description of the procedure for the Revenue Code billed. If the patient is dual-eligible, the N4 indicator first, then the 11-digit NDC code. In the third place, list the quantity and, last, the unit measurement code. Check with other payers for their requirements.
An example for this products is N483831010220MG.

FL 43

FL 44 (Electronic Claim Form = Loop 2400, SV202-1=HC/HP):
Enter the appropriate HCPCS code, code, J9172, Injection, docetaxel not therapeutically equivalent to J9171, 1 mg.
For administration, enter the appropriate code or codes for the infusion duration. As an example, a 60-minute infusion of chemotherapy requires 96413.*

FL 44

FL 45 (Electronic Claim Form = Loop 2400, Segment DTP/472/03):
Enter the date of service.

FL 45

FL 46 (Electronic Claim Form = Loop 2400, SV205):
Enter the units for the HCPCS code billed. Enter the number of service units for each item: 20 units if using a carton of 1 single-dose vial 20 mg/2mL (10 mg/mL).

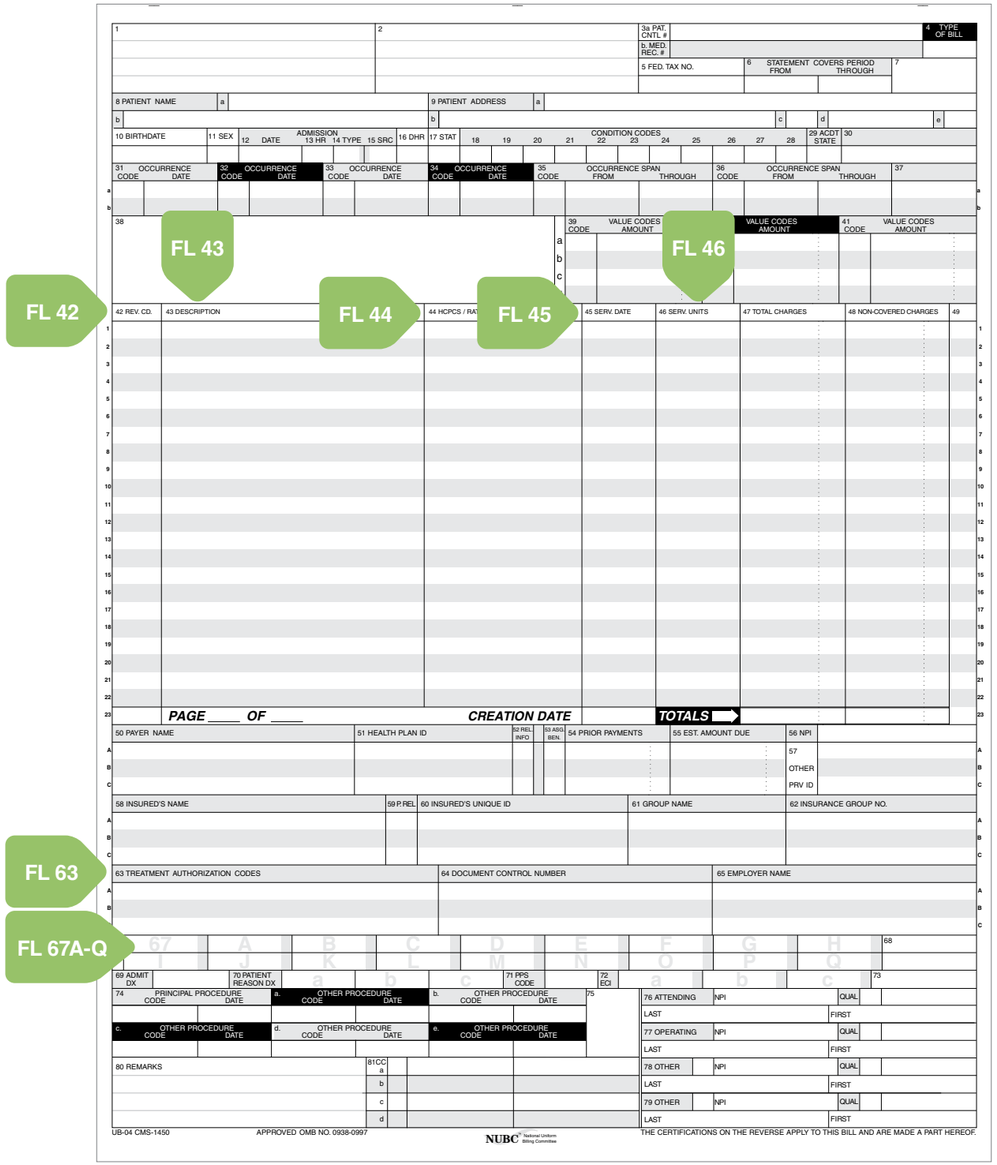
FL 46

FL 63 (Electronic Claim Form = Loop 2300,REF/G1/02):
Enter treatment authorization code.

FL 63

FL 67A-Q (Electronic Claim Form = Loop 2300, HI01-2 (HI01-1=BK):
Enter a diagnosis code for the drug documented in the medical record. Be as specific as possible.
The code listed here is an example: C50.111, Malignant neoplasm of central portion of right female breast.

FL 67A-Q



*CPT Code 96413 Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug. Initial infusion times may vary.

CMS: Centers for Medicare & Medicaid Services; HCPCS: Healthcare Common Procedure Coding System; NDC: National Drug Code

CPT: Current Procedural Terminology

Please see Important Safety Information on pages 3, 4 and 14-21 and full Prescribing Information for DOCIVYX including BOXED WARNING.

DOCIVYX™
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Sample Claim Form CMS-1500[8]

This information is provided for educational purposes only and is not a guarantee of coverage. It is the sole responsibility of the healthcare professional to select the proper codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

Box 21 (Electronic Claim Form = Loop 2300, Segment H101-2 through H112=2):
Enter the patient's diagnosis from the patient's medical record. An example code for this drug is C50.11, Malignant neoplasm of central portion of right female breast
Use Box 21 B-L fields for secondary diagnoses.

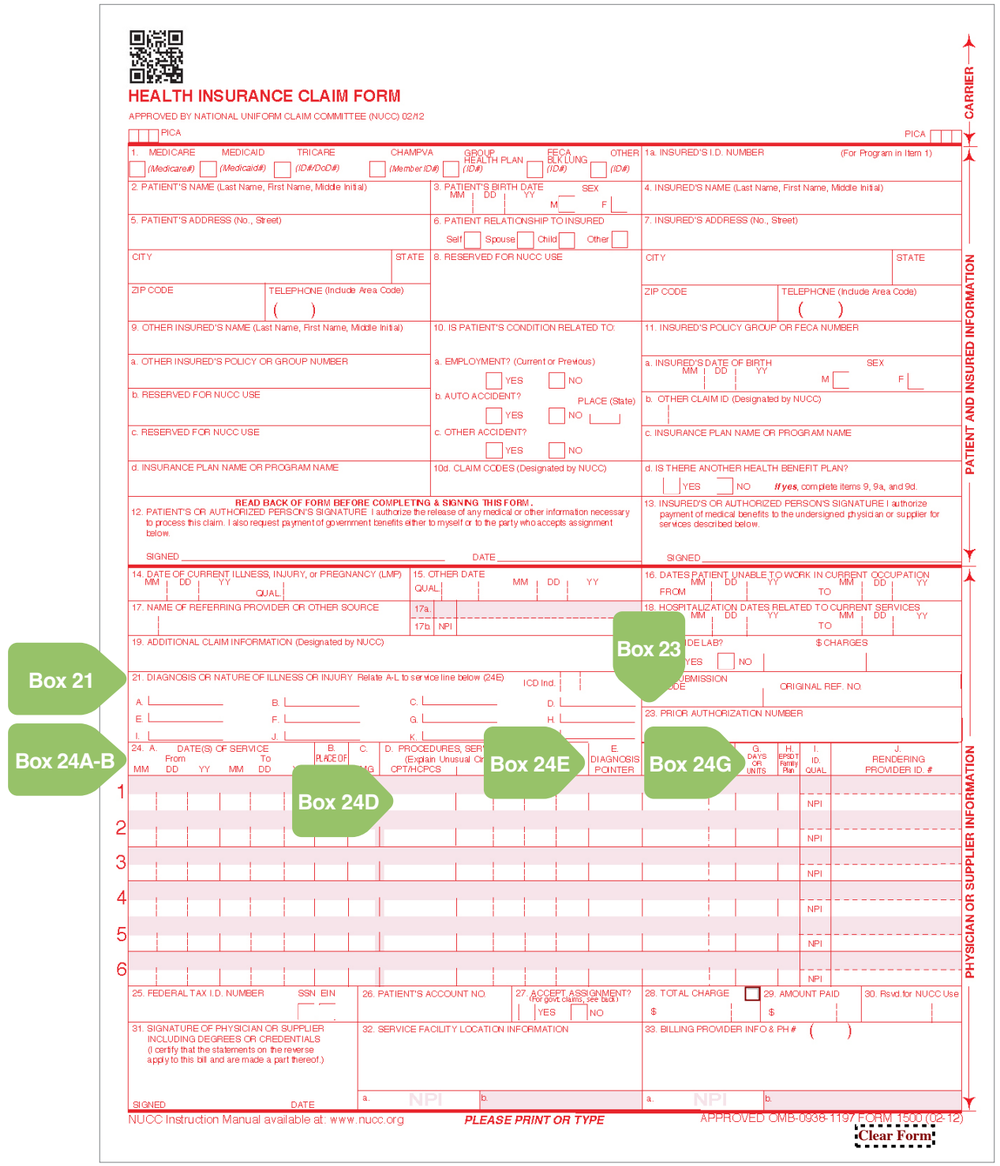
Box 23 (Electronic Claim Form = Loop 2300, REF02):
Enter prior authorization number if one exists.

Box 24A-B (Electronic Claim Form):
Box 24A (Electronic Claims Form = Loop 2400, DTP02; Box 24B (Loop 2300/2400, Segment CLM05-1/SV105)
In the non-shaded area, enter the appropriate date of service and place of service code. Example: Office = 11
In the shaded area, enter the N4 indicator first, then the 11 digit NDC code. In the third space, list the quantity and, last, the unit measurement code.
An example for this drug is N483831010220MG

Box 24D (Electronic Claim Form = Loop 2400, Segment SV101):
Enter the appropriate HCPCS code, J9172, Injection, docetaxel not therapeutically equivalent to J9171, 1 mg.
For administration, enter the appropriate code or codes for the infusion duration. As an example, a 60-minute infusion of chemotherapy requires 96413.*

Box 24E (Electronic Claim Form = Loop 2400, Segment SV107):
Specify the diagnosis letter that corresponds with the drug and drug administration code(s) in Box 21.

Box 24G (Electronic Claim Form = Loop 2400, SV104):
Enter the number of service units for each item.



*CPT Code 96413 Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug. Initial infusion times may vary.

CMS: Centers for Medicare & Medicaid Services; HCPCS: Healthcare Common Procedure Coding System NDC: National Drug Code

CPT: Current Procedural Terminology

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INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (CONTINUED)

WARNINGS AND PRECAUTIONS

Toxic Deaths

Breast Cancer

DOCIVYX 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

DOCIVYX 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 DOCIVYX 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 DOCIVYX dose modifications. Measure bilirubin, AST or ALT, and alkaline phosphatase prior to each cycle of DOCIVYX therapy.

Hematologic Effects

Perform frequent peripheral blood cell counts on all patients receiving DOCIVYX. Do not retreat patients with subsequent cycles of DOCIVYX 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 DOCIVYX 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 DOCIVYX cycle.

Neutropenia (<2000 neutrophils/mm^3) occurs in virtually all patients given 60 mg/m^2 to 100 mg/m^2 of DOCIVYX 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. DOCIVYX 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 DOCIVYX 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 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 DOCIVYX infusion and aggressive therapy. Do not rechallenge patients with a history of severe hypersensitivity reactions with DOCIVYX.

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 DOCIVYX therapy. Hypersensitivity reactions may occur within a few minutes following initiation of a DOCIVYX 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 DOCIVYX.

Fluid Retention

Severe fluid retention has been reported following DOCIVYX therapy. Patients should be premedicated with oral corticosteroids prior to each DOCIVYX 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 DOCIVYX 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 DOCIVYX, 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 DOCIVYX 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.

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 DOCIVYX. Patients with impaired vision should undergo a prompt and comprehensive ophthalmologic examination. If CME is diagnosed, DOCIVYX treatment should be discontinued and appropriate treatment initiated. Alternative non-taxane cancer treatment should be considered.

INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (CONTINUED)

INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (CONTINUED)

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

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. Based on findings in animal studies and its mechanism of action, DOCIVYX can cause fetal harm when administered to a pregnant woman.

DOCIVYX contains alcohol which is associated with fetal harm including central nervous system abnormalities, behavioral disorders, and impaired intellectual development.

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 DOCIVYX. Advise females of reproductive potential to use effective contraception during treatment and for 2 months after the last dose of DOCIVYX. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of DOCIVYX.

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 DOCIVYX 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 DOCIVYX on the ability to drive or use machines immediately after the infusion. Each administration of DOCIVYX at 100 mg/m^2 delivers 2.0 g/m^2 of ethanol. For a patient with a BSA of 2.0 m^2, this would deliver 4.0 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 DOCIVYX and periodically during treatment. Correction of dehydration and treatment of high uric acid levels are recommended prior to initiation of treatment.

ADVERSE REACTIONS

The most serious adverse reactions from DOCIVYX 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.

The most common adverse reactions across all DOCIVYX 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 DOCIVYX 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 DOCIVYX 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%, 18%, respectively), hypersensitivity reactions with 3-day premedication (sever; 2%, 0%, 2%, respectively), hypersensitivity reactions with 3-day premedication (any; 15%, 33%, 15%, respectively), fluid retention regardless

Please see Important Safety Information on pages 3, 4 and 14-21 and full Prescribing Information for DOCIVYX including BOXED WARNING.

INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (CONTINUED)

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 DOCIVYX 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 DOCIVYX 100 mg/m^2 or those with normal liver function tests who were treated with DOCIVYX 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).

Hematologic adverse reactions (any) occurring in breast cancer patients previously treated with chemotherapy with normal or elevated liver function tests who were treated with DOCIVYX 100 mg/m^2 or those with normal liver function tests who were treated with DOCIVYX 60 mg/m^2 were neutropenia <2,000 cells/mm^3 (98%,100%, and 95% at 100 mg/m^2 with normal liver function tests, 100 mg/m^2 with elevated liver function tests, and at 60 mg/m^2 with normal liver function tests, respectively), thrombocytopenia <100,000 cells/mm^3 (11%,44%,14%, respectively), anemia <11 g/dL (95%,94%,65%, respectively), and infection (23%,39%,1%, 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 DOCIVYX 100 mg/m^2 or those with normal liver function tests who were treated with DOCIVYX 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 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).

Non-hematologic adverse reactions (any) occurring in breast cancer patients previously treated with chemotherapy with normal or elevated liver function tests who were treated with DOCIVYX 100 mg/m^2 or those with normal liver function tests who were treated with DOCIVYX 60 mg/m^2 were acute hypersensitivity reaction regardless of premedication (13% ,6%, and 1% 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), fluid retention regardless of premedication (56%,61%,13, respectively), neurosensory (57%,50%,20%, respectively), myalgia (23%,33%,3%, respectively), cutaneous (45%,61%,31%, respectively), asthenia (65%,44%,66%, respectively), diarrhea (42%,28%,NA, respectively), and stomatitis (53%,67%,19%, respectively).

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

Monotherapy trial (TAX313) comparing DOCIVYX 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 DOCIVYX in the adjuvant treatment of breast cancer

Adverse reactions (Grade 3/4) occurring in patients with breast cancer who were treated with DOCIVYX 75 mg/m^2

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INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (CONTINUED)

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%).

Adverse reactions (any) occurring in patients with breast cancer who were treated with DOCIVYX 75 mg/m^2 every 3 weeks in combination with doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 (TAX316) were anemia (92%), neutropenia (71%), fever in the absence of infection (47%), infection (39%), thrombocytopenia (39%), febrile neutropenia (25%), neutropenic infection (12%), hypersensitivity reactions (13%), lymphedema (4%), fluid retention (35%), peripheral edema (27%), weight gain (13%), neuropathy sensory (26%), neuro-cortical (5%), neuropathy motor (4%), neuro-cerebellar (2%), syncope (2%), alopecia (98%), skin toxicity (27%), nail disorders (19%), nausea (81%), stomatitis (69%), vomiting (45%), diarrhea (35%), constipation (34%), taste perversion (28%), anorexia (22%), abdominal pain (11%), amenorrhea (62%), cough (14%), cardiac dysrhythmias (8%), vasodilation (27%), hypotension (2%), phlebitis (1%), asthenia (81%), myalgia (27%), arthralgia (19%), lacrimation disorder (11%), and conjunctivitis (5%).

Monotherapy with DOCIVYX 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 DOCIVYX 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%).

Adverse reactions (any) occurring in patients with locally advanced or metastatic NSCLC and a history of prior treatment with platinum-based chemotherapy who were treated with DOCIVYX 75 mg/m^2 monotherapy were neutropenia (84%), leukopenia (84%), thrombocytopenia (8%), anemia (91%), infection (34%), hypersensitivity reactions (6%), fluid retention (34%), neurosensory (23%), neuromotor (16%), skin (20%), nausea (34%), vomiting (22%), diarrhea (23%), alopecia (56%), asthenia (53%), stomatitis (26%), pulmonary (41%), nail disorder (11%), myalgia (6%), arthralgia (3%), and taste perversion (6%).

Combination therapy with DOCIVYX 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 DOCIVYX 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%).

Adverse reactions (any) occurring in patients with advanced unresectable or metastatic NSCLC and no history of prior chemotherapy who were treated with DOCIVYX 75 mg/m^2 in combination with cisplatin 75 mg/m^2 (TAX326) were neutropenia (91%), febrile neutropenia (5%), thrombocytopenia (15%), anemia (89%), infection (35%), fever in the absence of infection (33%), hypersensitivity reaction (12%), fluid retention (54%), pleural effusion (23%), peripheral edema (34%), weight gain (15%), neurosensory (47%), neuromotor (19%), skin reaction (16%), nausea (72%), vomiting (55%), diarrhea (47%), anorexia (42%), stomatitis (24%), alopecia (75%), asthenia (74%), nail disorders (14%), and myalgia (18%).

Combination therapy with DOCIVYX in patients with castration-resistant prostate cancer (CRPC)

Adverse reactions (Grade 3/4) occurring in patients with CRPC who were treated with DOCIVYX 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%).

Adverse reactions (any) occurring in patients with CRPC who were treated with DOCIVYX 75 mg/m^2 every 3 weeks in combination with prednisone 5 mg orally twice daily (TZX327) were anemia (67%), neutropenia (41%),

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INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (CONTINUED)

thrombocytopenia (3%), febrile neutropenia (3%), infection (32%), epistaxis (6%), allergic reactions (8%), fluid retention (24%), weight gain (8%), peripheral edema (18%), neuropathy sensory (30%), neuropathy motor (7%), rash or desquamation (6%), alopecia (65%), nail changes (30%), nausea (41%), diarrhea (32%), stomatitis/pharyngitis (20%), taste disturbance (18%), vomiting (17%), anorexia (17%), cough (12%), dyspnea (15%), cardiac left ventricular function (10%), fatigue (53%), myalgia (15%), tearing (10%), and arthralgia (8%).

Combination therapy with DOCIVYX 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 DOCIVYX 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%).

Adverse reactions (any) occurring in patients with advanced gastric adenocarcinoma and no history of prior chemotherapy for advanced disease who were treated with DOCIVYX 75 mg/m^2 in combination with cisplatin 75 mg/m^2 and fluorouracil 750 mg/m^2 were anemia (97%), neutropenia (96%), fever in the absence of infection (36%), thrombocytopenia (26%), infection (29%), febrile neutropenia (16%), neutropenic infection (16%), allergic reactions (10%), fluid retention (15%), edema (13%), lethargy (63%), neurosensory (38%), neuromotor (9%), dizziness (16%), alopecia (67%), rash/itch (12%), nail changes (8%), skin desquamation (2%), nausea (73%), vomiting (67%), anorexia (51%), stomatitis (59%), diarrhea (78%), constipation (25%), esophagitis/dysphagia/odynophagia (16%), gastrointestinal pain/cramping (11%), cardiac dysrhythmias (5%), myocardial ischemia (1%), tearing (8%), and altered hearing (6%).

Combination therapy with DOCIVYX 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 DOCIVYX 75 mg/m^2 in combination with cisplatin 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).

Adverse reactions (any) occurring in patients with SCCHN who received induction chemotherapy with DOCIVYX 75 mg/m^2 in combination with cisplatin 75 mg/m^2 and fluorouracil 750 mg/m^2 followed by radiotherapy (TAX323) or chemoradiotherapy (TAX 324), respectively, were neutropenia (93%, 95% with combination therapy followed by radiotherapy [TAX323] or chemoradiotherapy [TAX324], respectively), anemia (89%,90%, respectively), thrombocytopenia (24%,28%, respectively), infection (27%,23%, respectively), febrile neutropenia (5%,12%, respectively), neutropenic infection (14%,12%, respectively), cancer pain (21%,17%, respectively), lethargy (41%,61%, respectively), fever in the absence of infection (32%,30%, respectively), myalgia (10%,7%, respectively), weight loss (21%,14%, respectively), allergy (6%,2%, respectively), fluid retention (20%,13%, respectively), edema (13%,12%, respectively), weight gain (6%,0%, respectively), dizziness (2%,16%, respectively), neurosensory (18%,14%, respectively), altered hearing (6%,13%, respectively), neuromotor (2%,9%, respectively), alopecia (81%,68%, respectively), rash/itch (12%,20%, respectively), dry skin (6%,5%, respectively), desquamation (4%,2%, respectively) nausea (47%,77%, respectively), stomatitis (43%,66%, respectively), vomiting (26%,56%, respectively), diarrhea (33%, 48%, respectively),

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constipation (17%,27%, respectively), anorexia (16%,40%, respectively), esophagitis/dysphagia/odynophagia (13%,25%, respectively), taste, sense of smell altered (10%,20%, respectively), gastrointestinal pain/cramping (8%,15%, respectively), heartburn (6%,13%, respectively), gastrointestinal bleeding (4%,5%, respectively), cardiac dysrhythmia (2%,6%, respectively), venous (3%,4%, respectively), ischemia myocardial (2%,2%, respectively), tearing (2%,2%, respectively), and conjunctivitis (1%,1%, respectively).

Postmarketing Experience

The following adverse reactions have been identified from clinical trials and/or postmarketing surveillance. Because these reactions are reported from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Body as a whole: diffuse pain, chest pain, radiation recall phenomenon, injection site recall reaction (recurrence of skin reaction at a site of previous extravasation following administration of docetaxel at a different site) at the site of previous extravasation.

Cardiovascular: atrial fibrillation, deep vein thrombosis, ECG abnormalities, thrombophlebitis, pulmonary embolism, syncope, tachycardia, myocardial infarction. Ventricular arrhythmia, including ventricular tachycardia, in patients treated with docetaxel in combination regimens including doxorubicin, 5-fluorouracil and/or cyclophosphamide may be associated with fatal outcome.

Cutaneous: cutaneous lupus erythematosus, bullous eruptions such as erythema multiforme and severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome, toxic epidermal necrolysis and acute generalized exanthematous pustulosis, scleroderma-like changes (usually preceded by peripheral lymphedema), severe palmar-plantar erythrodysesthesia, and permanent alopecia.

Gastrointestinal: enterocolitis, including colitis, ischemic colitis, and neutropenic enterocolitis, which may be fatal. Abdominal pain, anorexia, constipation, duodenal ulcer, esophagitis, gastrointestinal hemorrhage, gastrointestinal perforation, intestinal obstruction, ileus, and dehydration as a consequence of gastrointestinal events.

Hearing: ototoxicity, hearing disorders and/or hearing loss, including during use with other ototoxic drugs.

Hematologic: bleeding episodes, disseminated intravascular coagulation (DIC), often in association with sepsis or multiorgan failure.

Hepatic: hepatitis, sometimes fatal, primarily in patients with pre-existing liver disorders.

Hypersensitivity: anaphylactic shock with fatal outcome in patients who received premedication. Severe hypersensitivity reactions with fatal outcome with docetaxel in patients who previously experienced hypersensitivity reactions to paclitaxel.

Metabolism and nutrition disorders: electrolyte imbalance, including hyponatremia, hypokalemia, hypomagnesemia, and hypocalcemia. Tumor lysis syndrome, sometimes fatal.

Neurologic: confusion, seizures or transient loss of consciousness, sometimes appearing during the infusion of the drug.

Ophthalmologic: conjunctivitis, lacrimation or lacrimation with or without conjunctivitis, cystoid macular edema (CME). Excessive tearing which may be attributable to lacrimal duct obstruction. Transient visual disturbances (flashes, flashing lights, scotomata), typically occurring during drug infusion and reversible upon discontinuation of the infusion, in association with hypersensitivity reactions.

Respiratory: dyspnea, acute pulmonary edema, acute respiratory distress syndrome/pneumonitis, interstitial lung disease, interstitial pneumonia, respiratory failure, and pulmonary fibrosis, which may be fatal. Radiation pneumonitis in patients receiving concomitant radiotherapy.

Renal: renal insufficiency and renal failure, the majority of cases were associated with concomitant nephrotoxic drugs.

Second primary malignancies: second primary malignancies, including AML, MDS, NHL, and renal cancer.

Musculoskeletal disorder: myositis.

USE IN SPECIFIC POPULATIONS

Pregnancy

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. Based on findings in animal studies and its mechanism of action, DOCIVYX can cause fetal harm when administered to a pregnant woman. DOCIVYX contains alcohol which is associated with fetal harm including central nervous system abnormalities, behavioral disorders, and impaired intellectual development.

Lactation

There is no information regarding the presence of docetaxel

Please see Important Safety Information on pages 3, 4 and 14-21 and full Prescribing Information for DOCIVYX including BOXED WARNING.

INDICATIONS AND IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (CONTINUED)

in human milk, or on its effects on milk production or the breastfed child. Advise women not to breastfeed during treatment with DOCIVYX and for 1 week after the last dose.

Females and Males of Reproductive Potential

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

Pediatric Use

The alcohol content of DOCIVYX should be taken into account when given to pediatric patients. The efficacy of DOCIVYX in pediatric patients as monotherapy or in combination has not been established. The overall safety profile of DOCIVYX 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 DOCIVYX plus 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 DOCIVYX+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 DOCIVYX 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 DOCIVYX+cisplatin, and a higher frequency of diarrhea, infection and peripheral edema than elderly patients treated with vinorelbine+cisplatin.

Prostate Cancer

In patients ≥65 years of age with prostate cancer treated with DOCIVYX 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 and Head and Neck Cancer

The number of patients ≥65 years of age with breast cancer patients who received DOCIVYX in combination with doxorubicin and cyclophosphamide and the number of head and neck cancer patients who received DOCIVYX in combination with cisplatin and fluorouracil were not sufficient to determine whether elderly and younger patients responded differently.

Gastric Cancer

The number of patients ≥65 years of age with gastric cancer treated with DOCIVYX 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 DOCIVYX 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 DOCIVYX should be taken into account when given to patients with hepatic impairment.

Please see the full Prescribing information for safety information, including BOXED WARNING, and dosing guidelines.

To report SUSPECTED ADVERSE REACTIONS, contact Avyxa Pharma, LLC at 1-888-520-0954 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.com.

DOCIVYX™
(docetaxel) injection

Notes

Please see Important Safety Information on pages 3, 4 and 14-21 and full Prescribing Information for DOCIVYX including BOXED WARNING.

DOCIVYX™
(docetaxel) injection

References: 1. DOCIVYX™ [prescribing information]. Parsippany, NJ: AVYXA™ Pharma 2025. **2.** Centers for Medicare and Medicaid Services (2025, February 28). HCPCS Quarterly Update - April 2025 Alpha-Numeric HCPCS File. https://www.cms.gov/medicare/coding-billing/healthcare-common-procedure-system/quarterly-update. Accessed March 25, 2025. **3.** Centers for Medicare and Medicaid Services (2025, January 10). Healthcare Common Procedure Coding System (HCPCS). https://www.cms.gov/medicare/coding-billing/healthcare-common-procedure-system. Accessed March 25, 2025. **4.** Centers for Medicare and Medicaid Services (2023, November 1). Article - Billing and Coding: Approved Drugs and Biologicals; Includes Cancer Chemotherapeutic Agents (A53049). https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=53049&ver=98. Accessed March 25, 2025. **5.** Centers for Disease Control and Prevention (2024, October 1). ICD-10-CM Files - Fiscal Year Releases. https://www.cdc.gov/nchs/icd/icd-10-cm/files.html. Accessed March 25, 2025. **6.** Centers for Disease Control and Prevention (2024, October 1). ICD-10-CM Official Guidelines for Coding and Reporting FY 2025. https://stacks.cdc.gov/view/cdc/158747. Accessed March 25, 2025. **7.** Centers for Medicare and Medicaid Services. Medicare Claims Processing Manual. Chapter 25 – Completing and Processing the Form CMS 1450 Data Set. https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/clm104c25.pdf. Accessed March 25, 2025. **8.** Centers for Medicare and Medicaid Services. Medicare Claims Processing Manual. Chapter 26 – Completing and Processing the Form CMS 1500 Data Set. https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/clm104c26pdf.pdf. Accessed March 25, 2025

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