Paclitaxel Protein-Bound Particles

for Injectable Suspension (Albumin-Bound)

Billing & Coding Guide

Providers are solely responsible for ensuring compliance with Medicare, Medicaid, and all other third-party payer requirements, as well as accurate coding, documentation, and medical necessity for the services provided. Before filing claims, providers should confirm individual payer requirements and coverage/medical policies. The information provided in this document is not legal or coding advice; it is general reimbursement information for reference purposes only.

While we have attempted to be current as of the date of this document, the information may not be as current or comprehensive when you view it. You should always verify the appropriate reimbursement information for services or items you provide.

INDICATIONS AND USAGE

Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is a microtubule inhibitor indicated for the treatment of:

- Metastatic breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.
- Locally advanced or metastatic non–small cell lung cancer (NSCLC), as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.
- Metastatic adenocarcinoma of the pancreas, in combination with gemcitabine.

SELECT IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

WARNING: SEVERE MYELOSUPPRESSION

- **Do not administer Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) therapy to patients who have baseline neutrophil counts of less than 1,500 cells/mm^3.**
- **Monitor for neutropenia, which may be severe and result in infection or sepsis.**
- **Perform frequent complete blood cell counts on all patients receiving Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).**

CONTRAINDICATIONS

- Baseline neutrophil counts of <1500 cells/mm^3.
- A history of severe hypersensitivity reactions to Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).

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This brochure provides information that may be helpful in obtaining reimbursement for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).

Healthcare benefits vary significantly; therefore, it is important that healthcare provider offices verify each patient's insurance coverage prior to initiating therapy.

National Drug Code (NDC) for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

The NDC for Paclitaxel protein-bound particles is often required in addition to the appropriate J Code when filing a claim for reimbursement.

Paclitaxel Protein-Bound Particles for Injectable Suspension (Alubmin-Bound)	
Supplied as	100 mg/vial; single-dose vial
Shelf pack	1

Providers should check with their local payers to determine whether reporting requires the 10-digit vs. 11-digit NDC. Please see below:

NDCs	
10-digit:	0517-4300-01
11-digit:	00517-4300-01

NDCs may not be required for drugs with a product-specific HCPCS code under traditional Medicare, but must be included for drugs that are billed using a "miscellaneous" HCPCS code, such as C9399 or J9999, as part of the additional information that is reported on claims. Medicare Advantage plans may have different NDC reporting policies from traditional Medicare.

Providers should always check with their local payers to determine NDC reporting requirements.

Note: Providers are solely responsible for ensuring compliance with Medicare, Medicaid, and all other third-party payer requirements, as well as accurate coding, documentation, and medical necessity for the services provided. Before filing claims, providers should confirm individual payer requirements and coverage/medical policies. The information provided in this document is not legal or coding advice; it is general reimbursement information for reference purposes only.

Healthcare Common Procedure Coding System (HCPCS) and Revenue Codes for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

HCPCS codes are used for billing drugs and services to Medicare, Medicaid, and commercial payers. Effective July 1, 2023, the Centers for Medicare and Medicaid Services (CMS) established a new product-specific HCPCS code for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).

Recommended HCPCS code for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

HCPCS Code	Description
J9259	Injection, paclitaxel protein-bound particles, 1 mg

Billing unit conversion

1 mg	1 unit	100 mg vial	100 units

It is important to note that if less than the entire vial of paclitaxel protein-bound particles is administered, the remainder must be discarded. Current CMS policy for outpatient or office-administered drugs permits billing for the entire vial even if the entire contents are not used—but only if the unused portion is discarded and it is appropriately documented. The discarded amount is billed on a second claim line with a "JW" modifier.[1]

Revenue Codes[2] that may be used for the administration of Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) in the hospital

Revenue Code	Description
0250	General pharmacy
0258	IV Solutions; paclitaxel protein-bound particles administration
0260	IV Therapy (required by Medicare for separate billable drugs)
0636	Drugs requiring detailed coding; may be used to specify Paclitaxel protein-bound particles as the drug given

Current Procedural Terminology (CPT*) Codes for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

CPT codes are used to indicate which medical services and procedures were performed on a patient and/or how a drug or medical supply was adminsitered.

The following CPT codes may be used for administering paclitaxel protein-bound particles:

Recommended CPT code for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)[3]

CPT Code	Description
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance or drug

Note: Providers are solely responsible for ensuring compliance with Medicare, Medicaid, and all other third-party payer requirements, as well as accurate coding, documentation, and medical necessity for the services provided. Before filing claims, providers should confirm individual payer requirements and coverage/medical policies. The information provided in this document is not legal or coding advice; it is general reimbursement information for reference purposes only.

International Classification of Disease, 10th Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes

ICD-10-CM diagnosis codes are used to identify a patient's diagnosis and inform payers of why a service was provided.

ICD-10-CM is a seven-character, alphanumeric code. Each code begins with a letter, and that letter is followed by two numbers. The first three characters of ICD-10-CM are the "category." The category describes the general type of the injury or disease. The category is followed by a decimal point and the subcategory. This is followed by up to two subclassifications, which further explain the cause, manifestation, location, severity, and type of injury or disease. The last character is the extension.

The extension describes the type of encounter. That is, if this is the first time a healthcare provider has seen the patient for this condition/injury/disease, it's listed as the "initial encounter." Every encounter after the first is listed as a "subsequent encounter." Patient visits related to the effects of a previous injury or disease are listed with the term "sequela."

The ICD-10-CM diagnosis codes for the labeled indications for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) are provided on the following pages. Please verify with the payer as some health plans and Medicare insurers may specify which codes are covered under their policies. Please code to the level of specificity documented in the medical record.

ICD-10-CM Diagnosis Codes for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound): **Metastatic Breast Cancer**

ICD-10-CM Diagnosis Codes for Metastatic Breast Cancer[4]	
C50	Malignant neoplasm of breast
C50.0	Malignant neoplasm of nipple and areola
C50.01	Malignant neoplasm of nipple and areola, female
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.02	Malignant neoplasm of nipple and areola, male
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.1	Malignant neoplasm of central portion of breast
C50.11	Malignant neoplasm of central portion of breast, female
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.12	Malignant neoplasm of central portion of breast, male
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast

Continued on next page

ICD-10-CM Diagnosis Codes for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound): **Metastatic Breast Cancer** *(continued)*

ICD-10-CM Diagnosis Codes for Metastatic Breast Cancer	
C50.2	Malignant neoplasm of upper-inner quadrant of breast
C50.21	Malignant neoplasm of upper-inner quadrant of breast, female
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.22	Malignant neoplasm of upper-inner quadrant of breast, male
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.3	Malignant neoplasm of lower-inner quadrant of breast
C50.31	Malignant neoplasm of lower-inner quadrant of breast, female
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.32	Malignant neoplasm of lower-inner quadrant of breast, male
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.4	Malignant neoplasm of upper-outer quadrant of breast
C50.41	Malignant neoplasm of upper-outer quadrant of breast, female
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast

Continued on next page

ICD-10-CM Diagnosis Codes for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound): **Metastatic Breast Cancer** *(continued)*

ICD-10-CM Diagnosis Codes for Metastatic Breast Cancer	
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.42	Malignant neoplasm of upper-outer quadrant of breast, male
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.5	Malignant neoplasm of lower-outer quadrant of breast
C50.51	Malignant neoplasm of lower-outer quadrant of breast, female
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.52	Malignant neoplasm of lower-outer quadrant of breast, male
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.6	Malignant neoplasm of axillary tail of breast
C50.61	Malignant neoplasm of axillary tail of breast, female
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.62	Malignant neoplasm of axillary tail of breast, male

Continued on next page

ICD-10-CM Diagnosis Codes for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound): **Metastatic Breast Cancer** *(continued)*

ICD-10-CM Diagnosis Codes for Metastatic Breast Cancer	
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.8	Malignant neoplasm of overlapping sites of breast
C50.81	Malignant neoplasm of overlapping sites of breast, female
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.82	Malignant neoplasm of overlapping sites of breast, male
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.9	Malignant neoplasm of breast of unspecified site
C50.91	Malignant neoplasm of breast of unspecified site, female
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.92	Malignant neoplasm of breast of unspecified site, male
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast

Continued on next page

ICD-10-CM Diagnosis Codes for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound): **Advanced Non-Small Cell Lung Cancer**

ICD-10-CM Diagnosis Codes for Advanced Non-Small Cell Lung Cancer[4]	
C34.1	Malignant neoplasm of upper lobe, bronchus or lung
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
C34.3	Malignant neoplasm of lower lobe, bronchus or lung
C50.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C50.31	Malignant neoplasm of lower lobe, right bronchus or lung
C50.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.8	Malignant neoplasm of overlapping sites of bronchus and 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
C34.9	Malignant neoplasm of unspecified part of bronchus or 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 left bronchus or lung

ICD-10-CM Diagnosis Codes for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound): **Metastatic Pancreatic Adenocarcinoma**

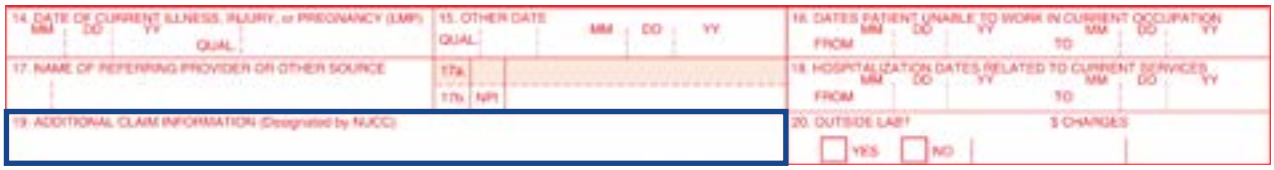
ICD-10-CM Diagnosis Codes for Metastatic Pancreatic Adenocarcinoma[4]	
C25	**Malignant neoplasm of pancreas**
C25.0	Malignant neoplasm of head of pancreas Malignant neoplasm of upper lobe, unspecified bronchus or lung
C25.1	Malignant neoplasm of body of pancreas Malignant neoplasm of upper lobe, right bronchus or lung
C25.2	Malignant neoplasm of tail of pancreas
C25.3	**Malignant neoplasm of pancreatic duct**
C25.4	**Malignant neoplasm of endocrine pancreas**
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	**Malignant neoplasm of overlapping sites of pancreas**
C25.9	Malignant neoplasm of pancreas, unspecified

CMS-1500 Form: Physician Office Sample Claim Form

Note: This Sample Form is presented for illustrative purposes only; it does not constitute advice or recommendation as to the correct coding choices to be used for each specific patient. Each provider is responsible for completing forms and choosing codes based upon services rendered and medical judgments made for each patient.

1 Item 19: Additional Claim Information

Payers typically require the drug name, total dosage and strength, method of administration, 11-digit NDC, and basis of measurement entered on Item 19.[5]



2 Item 21: Diagnosis Code(s)

Enter the appropriate ICD-10-CM diagnosis code(s) to describe the patient's condition; code reported should reflect the highest level of specificity.[5]

3 Item 24A: Date(s) of Service

Enter the date of service

Note: If NDC reporting is required, enter the NDC information in the shaded portion of Item 24A above the date of service. The NDC is preceded by the qualifier N4 and followed by the quantity qualifier (UN) and the quantity administered beginning in position 14.[5]

For example, use "N400517430001UN100" for one 100 mg vial of Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

Paclitaxel Protein-Bound Particles

for Injectable Suspension (Albumin-Bound)

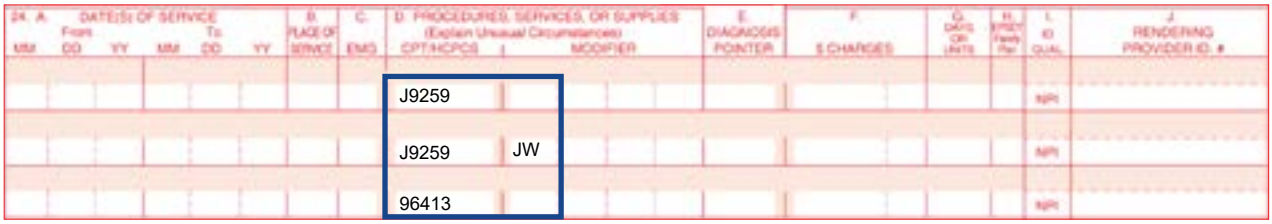
CMS-1500 Form: Physician Office Sample Claim Form *(continued)*

4 Item 24D: Product and Procedure Codes

Enter the appropriate HCPCS code (J9259). If you will be recording waste, it is required that you enter J9259-JW on the next line.[5]

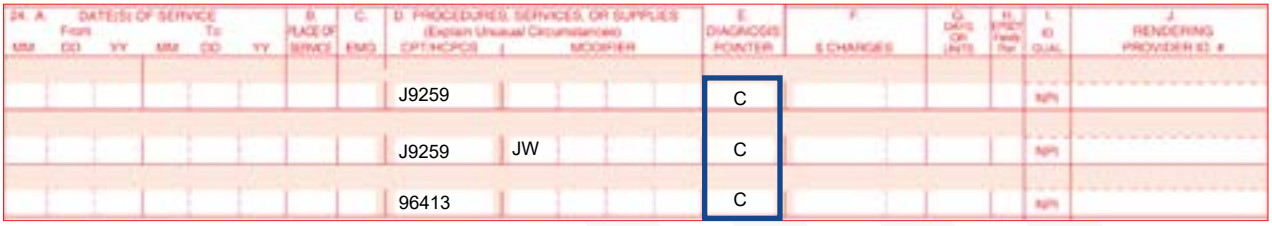
NOTE: American Regent's J code, J9259, Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) will be effective for dates of service on or after July 1, 2023.

Enter the appropriate CPT code(s) for drug administration services based on the actual service performed. For example, a chemotherapy IV infustion lasting at least 16 minutes would be reported using CPT code 96413 - Chemotherapy administration, intravenos infusion technique; up to 1 hour, single or initial substance/drug.



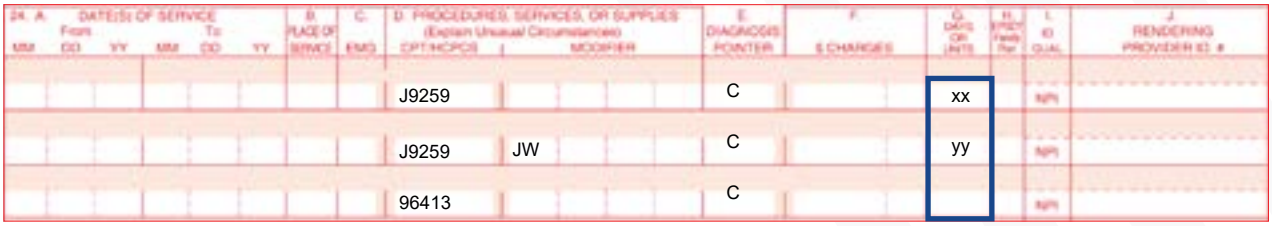
5 Item 24E: Diagnosis Pointer

Specify the diagnosis code reference letter from Item 21 that corresponds to each HCPCS or CPT code[5]



6 Item 24G: Service Units

Report units of service for each HCPCS code here. [8] For HCPCS J9259, 1 mg = 1 service unit. The service units for the line time with the JW modifier (when applicable) should reflect the unused portion of the 100 mg single-dose vial.



UB-04 (CMS-1450) Hospital Outpatient Sample Claim Form

Note: This Sample Form is presented for illustrative purposes only; it does not constitute advice or recommendation as to the correct coding choices to be used for each specific patient. Each provider is responsible for completing forms and choosing codes based upon services rendered and medical judgments made for each patient.

1 Form Locator (FL) 42: Revenue Codes

Enter the appropriate 4-digit revenue code that best describes the service provided, in accordance with hospital billing policy.[6] CMS recommends using revenue code 0636 (drugs requiring detailed coding).[6]

42 REV. CD.	43 DESCRIPTION	44 HCPCS / RATE / HIPPS CODE	45 SERV. DATE	46 SERV. UNITS	47 TOTAL CHARGES
0636					
0636					

2 FL 43: Description

If NDC reporting is required, enter the modifier "N4" followed by the 11-digit NDC in positions 01-13.[6] For example, use "N4005174300001UN100" for one 100 mg vial.

42 REV. CD.	43 DESCRIPTION	44 HCPCS / RATE / HIPPS CODE	45 SERV. DATE	46 SERV. UNITS	47 TOTAL CHARGES
0636	N400517430001UN100				
0636					

3 FL 44: Product and Procedure Codes

Enter the HCPCS code (J9529) and code for the outpatient service (and modifier[s], if applicable).[6] It is required that you enter J9259-JW on the next line to record waste if necessary.

NOTE: American Regent's J code, J9259, Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) will be effective for dates of service on or after July 1, 2023.

42 REV. CD.	43 DESCRIPTION	44 HCPCS / RATE / HIPPS CODE	45 SERV. DATE	46 SERV. UNITS	47 TOTAL CHARGES
0636	N400517430001UN100	J9259			
0636		J9259-JW			

UB-04 (CMS-1450) Hospital Outpatient Sample Claim Form *(continued)*

4 FL 46: Service Units

Enter the billing units (refered to as service units here) for each HCPCS code.[6] For HCPCS code J9259, 1 mg = 1 billing/service unit. The billing/service units for the line item with the JW modifier (when applicable), should reflect the unused portion of the 100 mg single-dose vial.

42 REV. CD.	43 DESCRIPTION	44 HCPCS / RATE / HIPPS CODE	45 SERV. DATE	46 SERV. UNITS	47 TOTAL CHARGES
0636	N400517430001UN100	J9259		xx	
0636		J9259-JW		yy	

5 FL 67: Diagnosis Code

Enter the appropriate ICD-10-CM diagnosis code(s) to describe the patient's condition; code reported should reflect the highest level of specificity.[6]

66 DX	A	B	C	D	E	F	G	H	68
C50.111									
I	J	K	L	M	N	O	P	Q	

6 FL 80: Remarks

Some payers require detailed information about the drug. The drug name, total dosage and strength, method of administration, 11 digit NDC, and basis of measurement are typically required in this section.[6]

80 REMARKS	81CC					
	a			78 OTHER	NPI	QUAL
	b			LAST		FIRST
	c			79 OTHER	NPI	QUAL
	d			LAST		FIRST

Please see Important Safety Information including **BOXED WARNING for severe myelosuppression** on pages 18-24 and accompanying Full Prescribing Information

AMERICAN REGENT®

Important Safety Information for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

For Intravenous Use

INDICATIONS AND USAGE

Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is a microtubule inhibitor indicated for the treatment of:

- Metastatic breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.
- Locally advanced or metastatic non–small cell lung cancer (NSCLC), as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.
- Metastatic adenocarcinoma of the pancreas, in combination with gemcitabine.

IMPORTANT SAFETY INFORMATION, INCLUDING BOXED WARNING

WARNING: SEVERE MYELOSUPPRESSION

- **Do not administer Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) therapy to patients who have baseline neutrophil counts of less than 1,500 cells/mm^3.**
- **Monitor for neutropenia, which may be severe and result in infection or sepsis.**
- **Perform frequent complete blood cell counts on all patients receiving Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).**

CONTRAINDICATIONS

- Baseline neutrophil counts of <1500 cells/mm^3.
- A history of severe hypersensitivity reactions to Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).

WARNINGS AND PRECAUTIONS

Severe Myelosuppression

- Severe myelosuppression (primarily neutropenia) is dose-dependent and a dose-limiting toxicity of protein-bound paclitaxel. In clinical studies, Grade 3-4 neutropenia occurred in 34% of patients with metastatic breast cancer (MBC), 47% of patients with non–small cell lung cancer (NSCLC), and 38% of patients with pancreatic cancer.
- Monitor for severe neutropenia and thrombocytopenia by performing complete blood cell counts frequently, including prior to dosing on Day 1 (for MBC) and Days 1, 8, and 15 (for NSCLC and for pancreatic cancer).
- Do not administer Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) to patients with baseline absolute neutrophil counts (ANC) of less than 1,500 cells/mm^3.
- In the case of severe neutropenia (<500 cells/mm^3 for 7 days or more) during a course of Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) therapy, reduce the dose of Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) in subsequent courses in patients with either MBC or NSCLC.

Important Safety Information for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

- In patients with MBC, resume treatment with every-3-week cycles of Paclitaxel Protein-Bound Particles after ANC recovers to a level >1500 cells/mm^3 and platelets recover to a level >100,000 cells/mm^3.
- In patients with NSCLC, resume treatment if recommended at permanently reduced doses for both weekly Paclitaxel Protein-Bound Particles and every-3-week carboplatin after ANC recovers to at least 1500 cells/mm^3 and platelet count of at least 100,000 cells/mm^3 on Day 1 or to an ANC of at least 500 cells/mm^3 and platelet count of at least 50,000 cells/mm^3 on Days 8 or 15 of the cycle.
- In patients with adenocarcinoma of the pancreas, withhold Paclitaxel Protein-Bound Particles and gemcitabine if the ANC is less than 500 cells/mm^3 or platelets are less than 50,000 cells/mm^3 and delay initiation of the next cycle if the ANC is less than 1500 cells/mm^3 or platelet count is less than 100,000 cells/mm^3 on Day 1 of the cycle. Resume treatment with appropriate dose reduction if recommended.

Severe Neuropathy

- Sensory neuropathy is dose- and schedule-dependent, occurs frequently and may require dose reduction or treatment interruption.
- If ≥ Grade 3 sensory neuropathy develops, withhold Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) treatment until resolution to Grade 1 or 2 for MBC or until resolution to ≤ Grade 1 for NSCLC and pancreatic cancer followed by a dose reduction for all subsequent courses.

Sepsis

- Sepsis occurred in 5% of patients with or without neutropenia who received protein-bound paclitaxel in combination with gemcitabine.
- Biliary obstruction or presence of biliary stent were risk factors for severe or fatal sepsis.
- If a patient becomes febrile (regardless of ANC), initiate treatment with broad-spectrum antibiotics.
- For febrile neutropenia, interrupt Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and gemcitabine until sepsis resolves, and if neutropenia, until neutrophils are at least 1500 cells/mm^3, then resume treatment at reduced dose levels.

Pneumonitis

- Pneumonitis, including some cases that were fatal, occurred in 4% of patients with or without neutropenia with the use of protein-bound paclitaxel in combination with gemcitabine.
- Monitor patients for signs and symptoms and interrupt Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and gemcitabine during evaluation of suspected pneumonitis.
- Permanently discontinue treatment with Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and gemcitabine upon making a diagnosis of pneumonitis.

Severe Hypersensitivity

- Severe and sometimes fatal hypersensitivity reactions, including anaphylactic reactions. Cross-hypersensitivity between protein-bound paclitaxel and other taxane products has been reported and may include severe reactions such as anaphylaxis. Closely monitor patients with a previous history of hypersensitivity to other taxanes during initiation of therapy.
- Do not rechallenge patients who experience a severe hypersensitivity reaction to Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) with this drug.

Please see Important Safety Information including **BOXED WARNING for severe myelosuppression** on pages 18-24 and accompanying Full Prescribing Information

Important Safety Information for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

Use in Patients with Hepatic Impairment

- Exposure and toxicity of paclitaxel can be increased in patients with hepatic impairment. Closely monitor patients with hepatic impairment for severe myelosuppression. Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is not recommended in patients who have a total bilirubin >5 x ULN or AST >10 x ULN.
- For MBC and NSCLC, the starting dose should be reduced for patients with moderate or severe hepatic impairment.
- For pancreatic adenocarcinoma, Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is not recommended for patients with moderate to severe hepatic impairment (total bilirubin >1.5 x ULN and AST ≤10 x ULN).

Albumin (Human)

- Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) contains albumin derived from human blood, which has a remote risk of viral transmission.

Embryo-Fetal Toxicity

- Can cause fetal harm when administered to a pregnant woman. (See Special Populations).
- Advise females of reproductive potential of the potential risk to a fetus.
- Advise females of reproductive potential to use effective contraception and avoid becoming pregnant during treatment with Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and for at least six months after the last dose of Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).
- Advise male patients with female partners of reproductive potential to use effective contraception and avoid fathering a child during treatment with Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and for at least three months after the last dose of Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).

ADVERSE REACTIONS

Randomized Metastatic Breast Cancer (MBC) Study

- The most common adverse reactions (≥20%) with single-agent use of Paclitaxel Protein-Bound Particles (Albumin-Bound) vs paclitaxel injection in the MBC study are alopecia (90%, 94%), neutropenia (all cases 80%, 82%; severe 9%, 22%), sensory neuropathy (any symptoms 71%, 56%; severe 10%, 2%), abnormal ECG (all patients 60%, 52%; patients with normal baseline 35%, 30%), fatigue/asthenia (any 47%, 39%; severe 8%, 3%), myalgia/arthralgia (any 44%, 49%; severe 8%, 4%), AST elevation (any 39%, 32%), alkaline phosphatase elevation (any 36%, 31%), anemia (any 33%, 25%; severe 1%, <1%), nausea (any 30%, 22%; severe 3%, <1%), diarrhea (any 27%, 15%; severe <1%, 1%), and infections (24%, 20%), respectively.
- Sensory neuropathy was the cause of discontinuation in 7/229 patients.
- Other adverse reactions of note with the use of Protein-Bound Paclitaxel vs paclitaxel injection included vomiting, fluid retention, mucositis, hypersensitivity reactions, thrombocytopenia, neutropenic sepsis, and injection site reactions. Dehydration and pyrexia were also reported.
- Overall 11% of patients experienced creatinine elevation, 1% severe.

Important Safety Information for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

- Ocular/visual disturbances occurred in 13% of all patients (n=366) treated with Protein-Bound Paclitaxel and 1% were severe.
- Severe cardiovascular events possibly related to single-agent protein-bound paclitaxel occurred in approximately 3% of patients and included cardiac ischemia/infarction, chest pain, cardiac arrest, supraventricular tachycardia, edema, thrombosis, pulmonary thromboembolism, pulmonary emboli, and hypertension.
- Cases of cerebrovascular attacks (strokes) and transient ischemic attacks have been reported.

Non–Small Cell Lung Cancer (NSCLC) Study

- The most common adverse reactions (≥20%) of protein-bound paclitaxel in combination with carboplatin are anemia, neutropenia, thrombocytopenia, alopecia, peripheral neuropathy, nausea, and fatigue.
- The most common serious adverse reactions of protein-bound paclitaxel in combination with carboplatin for NSCLC are anemia (4%) and pneumonia (3%).
- The most common adverse reactions resulting in permanent discontinuation of protein-bound paclitaxel are neutropenia (3%), thrombocytopenia (3%), and peripheral neuropathy (1%).
- The most common adverse reactions resulting in dose reduction of protein-bound paclitaxel are neutropenia (24%), thrombocytopenia (13%), and anemia (6%).
- The most common adverse reactions leading to withholding or delay in protein-bound paclitaxel dosing are neutropenia (41%), thrombocytopenia (30%), and anemia (16%).
- The following common (≥10% incidence) adverse reactions were observed at a similar incidence in protein-bound paclitaxel plus carboplatin–treated and paclitaxel injection plus carboplatin–treated patients: alopecia (56%), nausea (27%), fatigue (25%), decreased appetite (17%), asthenia (16%), constipation (16%), diarrhea (15%), vomiting (12%), dyspnea (12%), and rash (10%); incidence rates are for the protein bound paclitaxel plus carboplatin treatment group.
- Adverse reactions with a difference of ≥2%, Grade 3 or higher, with combination use of protein-bound paclitaxel and carboplatin vs combination use of paclitaxel injection and carboplatin in NSCLC are anemia (28%, 7%), neutropenia (47%, 58%), thrombocytopenia (18%, 9%), and peripheral neuropathy (3%, 12%), respectively.
- Adverse reactions with a difference of ≥5%, Grades 1-4, with combination use of protein-bound paclitaxel and carboplatin vs combination use of paclitaxel injection and carboplatin in NSCLC are anemia (98%, 91%), thrombocytopenia (68%, 55%), peripheral neuropathy (48%, 64%), edema peripheral (10%, 4%), epistaxis (7%, 2%), arthralgia (13%, 25%), and myalgia (10%, 19%), respectively.
- Neutropenia (all grades) was reported in 85% of patients who received protein-bound paclitaxel and carboplatin vs 83% of patients who received paclitaxel injection and carboplatin.

Pancreatic Adenocarcinoma Study

- Among the most common (≥20%) adverse reactions in the phase III study, those with a ≥5% higher incidence in the protein-bound paclitaxel/gemcitabine group compared with the gemcitabine group are neutropenia (73%, 58%), fatigue (59%, 46%), peripheral neuropathy (54%, 13%), nausea (54%, 48%), alopecia (50%, 5%), peripheral edema (46%, 30%), diarrhea (44%, 24%), pyrexia (41%, 28%), vomiting (36%, 28%), decreased appetite (36%, 26%), rash (30%, 11%), and dehydration (21%, 11%).

Please see Important Safety Information including **BOXED WARNING for severe myelosuppression** on pages 18-24 and accompanying Full Prescribing Information

Important Safety Information for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

- Of these most common adverse reactions, those with a ≥2% higher incidence of Grade 3-4 toxicity in the protein-bound paclitaxel/gemcitabine group compared with the gemcitabine group, respectively, are neutropenia (38%, 27%), fatigue (18%, 9%), peripheral neuropathy (17%, 1%), thrombocytopenia (13%, 9%), asthenia (7%, 4%) dehydration (7%, 2%), nausea (6%, 3%), diarrhea (6%, 1%), pyrexia (3%, 1%), vomiting (6%, 4%), decreased appetite (5%, 2%), and hypokalemia (4%, 1%).
- Thrombocytopenia (all grades) was reported in 74% of patients in the protein-bound paclitaxel/gemcitabine group vs 70% of patients in the gemcitabine group.
- The most common serious adverse reactions of protein-bound paclitaxel (with a ≥1% higher incidence) are pyrexia (6%), dehydration (5%), pneumonia (4%), and vomiting (4%) .
- The most common adverse reactions resulting in permanent discontinuation of protein-bound paclitaxel were peripheral neuropathy (8%), fatigue (4%), and thrombocytopenia (2%).
- The most common adverse reactions resulting in dose reduction of protein-bound paclitaxel are neutropenia (10%) and peripheral neuropathy (6%).
- The most common adverse reactions leading to withholding or delay in protein-bound paclitaxel dosing are neutropenia (16%), thrombocytopenia (12%), fatigue (8%), peripheral neuropathy (15%), anemia (5%), and diarrhea (5%) .
- Other selected adverse reactions with a ≥5% higher incidence for all-grade toxicity in the protein-bound paclitaxel/gemcitabine group compared to the gemcitabine group, respectively, are asthenia (19%, 13%), mucositis (10%, 4%), dysgeusia (16%, 8%), headache (14%, 9%), hypokalemia (12%, 7%), cough (17%, 7%), epistaxis (15%, 3%), urinary tract infection (11%, 5%), pain in extremity (11%, 6%), arthralgia (11%, 3%), myalgia (10%, 4%), and depression (12%, 6%).

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of protein-bound paclitaxel or with paclitaxel injection and may be expected to occur with protein-bound paclitaxel. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- *Hypersensitivity Reactions:* Severe and sometimes fatal hypersensitivity reactions. Cross-hypersensitivity between protein bound and other taxanes has been reported.
- *Cardiovascular:* Congestive heart failure, left ventricular dysfunction, and atrioventricular block.
- *Respiratory:* Pneumonitis, interstitial pneumonia, pulmonary embolism, radiation pneumonitis, lung fibrosis.
- *Neurologic:* Cranial nerve palsies, vocal cord paresis, autonomic neuropathy resulting in paralytic ileus.
- *Vision Disorders:* Reduced visual acuity due to cystoid macular edema. Abnormal visual evoked potentials suggest persistent optic nerve damage.
- *Hepatic:* Hepatic necrosis and hepatic encephalopathy leading to death.
- *Gastrointestinal:* Intestinal obstruction, intestinal perforation, pancreatitis, ischemic colitis, neutropenic enterocolitis.
- *Injection Site Reaction:* Extravasation. Severe events such as phlebitis, cellulitis, induration, necrosis, and fibrosis.

Important Safety Information for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

Recurrence of skin reactions at a site of previous extravasation following administration of paclitaxel injection at a different site.

- *Metabolic and Nutritional Disorders*: Tumor lysis syndrome.
- *Other Clinical Events:* Skin reactions including generalized or maculopapular rash, erythema, and pruritus. Photosensitivity reactions, radiation recall phenomenon, scleroderma, and in some patients previously exposed to capecitabine, reports of palmar-plantar erythrodysesthesia. Stevens-Johnson syndrome and toxic epidermal necrolysis. Conjunctivitis, cellulitis, and increased lacrimation.
- *Accidental Exposure:* Upon inhalation of paclitaxel, dyspnea, chest pain, burning eyes, sore throat, and nausea. Following topical exposure, tingling, burning, and redness.

DRUG INTERACTIONS

- Caution should be exercised when administering Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) concomitantly with medicines known to inhibit or induce either CYP2C8 or CYP3A4.

USE IN SPECIFIC POPULATIONS

Pregnancy

- Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) can cause fetal harm when administered to a pregnant woman. Advise females of the potential risk to a fetus and to avoid becoming pregnant while receiving protein-bound paclitaxel.

Lactation

- Nursing must be discontinued when receiving treatment with Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and for two weeks after the last dose.

Females and Males of Reproductive Potential

- Based on animal studies and mechanism of action, Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) can cause fetal harm when administered to a pregnant woman.
- Verify the pregnancy status of females of reproductive potential prior to starting treatment.
- Advise females of reproductive potential to use effective contraception and avoid becoming pregnant during treatment with and for at least six months after the last dose of Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound).
- Advise males with female partners of reproductive potential to use effective contraception and avoid fathering a child during treatment with Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and for at least three months after the last dose.
- Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) may impair fertility in females and males of reproductive potential.

Pediatric

- The safety and effectiveness in pediatric patients have not been established.

Geriatric

Please see Important Safety Information including **BOXED WARNING for severe myelosuppression** on pages 18-24 and accompanying Full Prescribing Information

Important Safety Information for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

- A higher incidence of epistaxis, diarrhea, dehydration, fatigue, and peripheral edema was found in patients 65 years or older who received protein-bound paclitaxel for MBC in a pooled analysis of clinical studies.
- Myelosuppression, peripheral neuropathy, and arthralgia were more frequent in patients ≥65 years of age treated with protein-bound paclitaxel and carboplatin in NSCLC.
- Diarrhea, decreased appetite, dehydration, and epistaxis were more frequent in patients 65 years or older compared with patients younger than 65 years old who received protein-bound paclitaxel and gemcitabine in adenocarcinoma of the pancreas.

Renal Impairment

- There are insufficient data to permit dosage recommendations in patients with severe renal impairment or end stage renal disease (estimated creatinine clearance <30 mL/min).

Hepatic Impairment

- Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is not recommended for use in patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment.

OVERDOSAGE

- There is no known antidote for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) overdosage. The primary anticipated complications of overdosage would consist of bone marrow suppression, sensory neurotoxicity, and mucositis.

DOSAGE AND ADMINISTRATION

- **DO NOT SUBSTITUTE FOR OR WITH OTHER NON-PROTEIN BOUND PACLITAXEL FORMULATIONS.** Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) has different dosage and administration instructions from other paclitaxel products.
- Dose reductions or discontinuation may be needed based on severe hematologic, neurologic, cutaneous, or gastrointestinal toxicity.
- Closely monitor the infusion site for extravasation or drug infiltration during administration.

Refer to full Prescribing Information for complete Dosage and Administration information.

For additional Important Safety Information, please see accompanying Full Prescribing Information.

To report adverse drug events (ADEs), please call1.888.532.7998. ADEs may also be reported to the FDA: visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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