

Pfizer Oncology together™

INJECTION
Zirabev®
bevacizumab-bvzr
Pfizer

ZIRABEV® Billing and Coding Guide



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Introduction

Pfizer Inc. has developed this reference guide to assist healthcare providers (HCPs) with understanding coding for ZIRABEV (bevacizumab-bvzr), a bevacizumab biosimilar approved for use in the United States for intravenous use.

The information provided in this document is intended for informational purposes only and is not a comprehensive description of potential coding requirements for ZIRABEV. Coding and coverage policies change periodically and often without notice. The HCP is solely responsible for determining coverage and reimbursement parameters and appropriate coding for treatment of his/her patients. The information provided should not be considered a guarantee of coverage or reimbursement for ZIRABEV.

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Making your patients' support needs a priority. Together.

At Pfizer Oncology Together, patient support is at the core of everything we do. We've gathered resources and developed tools to help patients and their loved ones throughout ZIRABEV treatment. From helping to identify financial assistance options to connecting patients to resources for emotional support, your patients' needs are our priority.*



Benefits Verification

We can help determine a patient's coverage and out-of-pocket costs.

Prior Authorization (PA) Assistance

We can coordinate with a patient's insurer to determine the PA requirements. After a PA request is submitted, we can follow up with the payer until a final outcome is determined.

Appeals Assistance

We can review the reasons for a denied claim and provide information on payer requirements. After an appeal is submitted, we can follow up with the payer until a final outcome is determined.

Billing and Coding Assistance for Injectable Products

For your patient claim submissions, we provide easy access to sample forms and template letters, along with billing and coding information for physician office and hospital outpatient settings of care.

Patient Financial Assistance

We can help patients understand their benefits and connect them with financial assistance resources.



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Coding Overview

In the physician office and hospital outpatient department sites of care, Medicare Administrative Contractors (MACs), private commercial payers, and Medicaid may recognize the following codes for reporting ZIRABEV on claim forms.

Coding for ZIRABEV

In the physician office and hospital outpatient department sites of care, Medicare, Medicaid, and private commercial payers typically recognize the following codes for reporting ZIRABEV and its administration on claim forms.

Effective for dates of service on and after October 1, 2019, HCPCS code Q5118 may be used to report ZIRABEV.

HCPCS Code ¹	Descriptor
Q5118	Injection, bevacizumab-bvzr, biosimilar, (Zirabev), 10 mg

Modifiers may be included on claims to provide additional information. Some payers may require modifiers JA to be reported, indicating the route of administration. The JW modifier is used to report the amount of the drug that is unused after administration to a patient. For Medicare and some payers, the unused amount should be reported on a separate line of the claim form, and the claim should include the drug code, modifier, and number of units discarded.² Additional modifiers may also be considered appropriate when submitting claims.

HCPCS Modifier ^{1,2}	Descriptor
JA	Intravenous administration
JW ^a	Drug amount discarded/not administered to any patient
JZ ^a	Zero drug amount discarded/not administered to any patient

^aUse of the JZ modifier (in situations where it applies) is required on Medicare claims with a date of service on or after 7/1/2023. An applicable claim without modifier JW or JZ may be rejected beginning on 10/1/2023.

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ZIRABEV National Drug Codes

National Drug Codes (NDCs) are unique 10-digit, 3-segment numbers used to identify drugs.³

Strength ⁴	Vial Size	10-Digit NDC
100 mg/4 mL	Single-dose vial	0069-0315-01
400 mg/16 mL	Single-dose vial	0069-0342-01

NDC Conversion Example

For reimbursement purposes, some payers may require the HCP to include NDCs on the claim form. For claims-reporting purposes, some payers may also require HCPs to convert the 10-digit NDC to an 11-digit NDC by adding a "0" (zero) where appropriate to create a 5-4-2 configuration. The zero is added in front of the first segment of numbers when the 10-digit format is the 4-4-2 configuration. See placement of the red zero in the example below.

Strength	Vial Size	10-Digit NDC	11-Digit NDC
100 mg/4 mL	Single-dose vial	0069-0315-01	<u>0</u> 0069-0315-01
400 mg/16 mL	Single-dose vial	0069-0342-01	<u>0</u> 0069-0342-01

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Coding for ZIRABEV Administration Services

Current Procedural Terminology (CPT®) codes define specific medical procedures performed by physicians.⁵
The following codes may be used to report the administration of ZIRABEV:

Type of Code	Code/Descriptor	Relevant Sites of Service
Administration: CPT® codes ⁵	96413: Chemotherapy administration, IV infusion technique; up to 1 hour, single or initial substance/drug	Physician office and hospital outpatient department
	96415: Chemotherapy administration, IV infusion technique; each additional hour (List separately in addition to code for primary procedure)	
	96417: Chemotherapy administration, IV infusion technique; each additional sequential infusion (different substance/drug), up to 1 hour (List separately in addition to code for primary procedure)	

Hospital outpatient departments use revenue codes to report specific accommodations and/or ancillary charges.⁶

Type of Code	Code/Descriptor	Relevant Sites of Service
Revenue codes ⁷	0636: Drugs requiring specific identification – detailed coding	Hospital outpatient department
	0500: Outpatient services – general classification	
	0510: Clinic – general classification	

Key: IV - intravenous

Current Procedural Terminology (CPT®) is a registered trademark of the American Medical Association.

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Diagnosis Coding for ZIRABEV

ZIRABEV (bevacizumab-bvzr) is an FDA-approved biosimilar.

The International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code set should be used, as appropriate, to report the patient-specific diagnosis.

Reporting the medical necessity for ZIRABEV may require a primary as well as secondary diagnosis, in some cases. HCPs should verify payer-specific coding requirements before submitting a claim and the order of required codes (eg, primary, secondary, etc), as these may vary by payer. ICD-10-CM codes may include, but are not limited to, the codes listed below:

ICD-10-CM Code ⁸	Descriptor
C18.0	Malignant neoplasm of the cecum
C18.1	Malignant neoplasm of appendix
C18.2–C18.9	Malignant neoplasm of the colon, various sites
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C33	Malignant neoplasm of trachea
C34.00–C34.02	Malignant neoplasm of main bronchus
C34.10–C34.12	Malignant neoplasm of upper lobe, bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30–C34.32	Malignant neoplasm of lower lobe, bronchus or lung
C34.80–C34.82	Malignant neoplasm of overlapping sites of bronchus and lung
C34.90–C34.92	Malignant neoplasm of unspecified part of bronchus or lung
C64.1–C64.2	Malignant neoplasm of right or left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C71.0–C71.9	Malignant neoplasm of brain
C53.0–C53.1	Malignant neoplasm of the endocervix or exocervix
C53.8–C53.9	Malignant neoplasm of overlapping sites of cervix uteri or unspecified sites of the cervix uteri
C56.1–C56.9	Malignant neoplasm of ovary
C57.00–C57.02	Malignant neoplasm of fallopian tube
C48.1–C48.8	Malignant neoplasm of specified parts of peritoneum, unspecified peritoneum, or overlapping sites of retroperitoneum and peritoneum

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ZIRABEV Billing Units

The ZIRABEV HCPCS code Q5118 is described as “Injection, bevacizumab-bvzr, biosimilar, (Zirabev), 10 mg.” Each dose increment of 10 milligrams equals 1 billing unit. For example, a 100 mg vial of ZIRABEV represents 10 billing units of Q5118. See the chart below correlating a vial of ZIRABEV administered with the number of billing units based on the description of Q5118.

Strength	Vial Size	Number of Q5118 Billing Units (10 mg bevacizumab-bvzr) Equivalent to the Milligrams of ZIRABEV in Each Vial
100 mg/4 mL	Single-dose vial	10 units
400 mg/16 mL	Single-dose vial	40 units

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Sample Claim Form: UB-04, Hospital Outpatient Site of Service

1	2	3a PAT. CNTL. #	4 TYPE OF BILL
3b REV. REC. #	5 FED. TAX NO.	6 STATEMENT COVERS PERIOD FROM	7 THROUGH
8 PATIENT NAME	9 PATIENT ADDRESS	10	11
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860	861	862	863
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968	969	970	971
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Form Locator (FL) 44: Specify appropriate HCPCS and CPT codes and modifiers; for example:

- Drug: Q5118 for ZIRABEV
- Administration: 96xxx for drug administration

This sample form is intended as a reference for the coding and billing of ZIRABEV. This form is not intended to be directive, and the use of the recommended codes does not guarantee reimbursement. HCPs may deem other codes or policies more appropriate and should select the coding options that most accurately reflect their internal guidelines, payer requirements, practice patients, and services rendered.

FL 46: Specify the billing units. For example, 1 billing unit = **10 mg** of bevacizumab-bvzr biosimilar (ZIRABEV) for HCPCS code Q5118. To bill 100 mg of ZIRABEV, enter 10 billing units. To bill 1 96xxx for drug administration, enter 1 billing unit

FL 42 and 43: Specify revenue codes and describe procedures; for example:

- 0636: Drugs requiring specific identification – detailed coding (For ZIRABEV)
- 0500: Outpatient services – general classification
- 0510: Clinic – general classification (For IV injection administered in the clinic)

Note: Other revenue codes may apply

FL 67: Specify appropriate ICD-10-CM diagnosis code(s)

FL 66: Identify the type of ICD diagnosis code used (eg, enter a “0” for ICD-10-CM)

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Claims Submission Checklist

The following may be considered to assist with submitting claims completely and accurately, which is important for timely claims processing, for appropriate payment, and to avoid denied claims.



- Provide the patient name, address, and insurance identification number, and review these for accuracy
- Include the HCP's name, National Provider Identifier (NPI), and payer-specific provider ID (if applicable)
- Indicate the appropriate place of service code (2-digit code) for where the treatment was provided
- Check to ensure that ICD-10-CM diagnosis codes, CPT procedure codes, and modifiers (if applicable) are consistent with information included in the patient's medical record
- Review the ZIRABEV-specific information (eg, name of drug, HCPCS code, NDC, number of units, route, and frequency of administration)

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IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- **Gastrointestinal Perforations and Fistulae.** Serious and sometimes fatal gastrointestinal perforation occurred at a higher incidence in patients receiving bevacizumab products compared to patients receiving chemotherapy. The incidence ranged from 0.3% to 3% across clinical studies. Non-GI fistulae incidence ranged from <1% to 1.8%, and was highest in patients with cervical cancer. Avoid ZIRABEV in patients with ovarian cancer who have evidence of recto-sigmoid involvement by pelvic examination or bowel involvement on CT scan or clinical symptoms of bowel obstruction. Discontinue for gastrointestinal perforations, tracheoesophageal fistula, grade 4 fistula, or fistula formation involving any internal organ
- **Surgery and Wound Healing Complications.** The incidence of wound healing and surgical complications, including serious and fatal complications, is increased in bevacizumab-treated patients. In patients who experience wound healing complications during ZIRABEV treatment, withhold ZIRABEV until adequate wound healing. Withhold for at least 28 days prior to elective surgery. Do not administer for at least 28 days following major surgery and until adequate wound healing. The safety of resumption of bevacizumab products after resolution of wound healing complications has not been established. Discontinue for wound healing complications of necrotizing fasciitis
- **Hemorrhage.** Severe or fatal hemorrhage, including hemoptysis, GI bleeding, hematemesis, central nervous system hemorrhage, epistaxis, and vaginal bleeding occurred up to 5-fold more frequently in patients receiving bevacizumab. In clinical studies, the incidence of grade ≥ 3 hemorrhagic events among patients receiving bevacizumab ranged from 0.4% to 7%. Do not administer ZIRABEV to patients with serious hemorrhage or a recent history of hemoptysis ($\geq 1/2$ tsp of red blood). Discontinue ZIRABEV in patients who develop grade 3-4 hemorrhage
- Additional serious and sometimes fatal adverse events with increased incidence in the bevacizumab-treated arm vs chemotherapy arm included:
 - **Arterial thromboembolic events (ATE)** (grade ≥ 3 , 5%, highest in patients with GBM). Discontinue in patients who develop a severe ATE
 - **Renal injury and proteinuria.** Monitor proteinuria during ZIRABEV therapy. Patients with a 2+ or greater urine dipstick reading should undergo 24-hour urine collection. Withhold for proteinuria ≥ 2 grams per 24 hours and resume when less than 2 grams per 24 hours. Discontinue in patients who develop nephrotic syndrome
 - Grade 3-4 proteinuria ranged from 0.7% to 7% in clinical studies
 - Nephrotic syndrome (<1%)
- Additional serious adverse events with increased incidence in the bevacizumab-treated arm vs chemotherapy arm included:
 - **Venous thromboembolism events (VTE)** (grade ≥ 3 , 11% seen in Study GOG-0240). Discontinue ZIRABEV in patients with a grade 4 VTE, including pulmonary embolism
 - **Hypertension** (grade 3-4, 5%-18%). Monitor blood pressure during treatment and, for ZIRABEV-associated hypertension, continue monitoring after discontinuation. Withhold for severe hypertension. Discontinue for hypertensive crisis or hypertensive encephalopathy
 - **Posterior reversible encephalopathy syndrome (PRES)** (<0.5%). Discontinue ZIRABEV in patients who develop PRES. Symptoms usually resolve or improve within days after discontinuing bevacizumab products, although some patients have experienced ongoing neurologic sequelae

- **Congestive heart failure (CHF)** (grade ≥ 3 left ventricular dysfunction, 1%). Discontinue ZIRABEV in patients who develop CHF
- **Infusion-related reactions.** Infusion-related reactions with the first dose of bevacizumab occurred in <3% of patients, and severe reactions occurred in 0.4% of patients. Decrease the rate of infusion for mild infusion-related reactions. Interrupt the infusion in patients with clinically significant infusion-related reactions and consider resuming at a slower rate following resolution. Discontinue in patients who develop a severe infusion-related reaction and administer appropriate medical therapy
- **Ovarian failure.** Inform females of reproductive potential of the risk of ovarian failure prior to initiating treatment with ZIRABEV

Pregnancy Warning

- Based on the mechanism of action and animal studies, bevacizumab products may cause fetal harm
- Advise female patients that bevacizumab products may cause fetal harm and to inform their health care provider of a known or suspected pregnancy
- Advise females of reproductive potential to use effective contraception during treatment with ZIRABEV and for 6 months after the last dose of ZIRABEV
- Advise nursing women that breastfeeding is not recommended during treatment with ZIRABEV and for 6 months following their last dose of treatment
- Bevacizumab products may impair fertility

Most Common Adverse Events

- Across studies, the most common adverse reactions observed in bevacizumab patients at a rate >10% were:
 - Epistaxis, headache, hypertension, rhinitis, proteinuria, taste alteration, dry skin, hemorrhage, lacrimation disorder, back pain, exfoliative dermatitis
- Across all studies, bevacizumab was discontinued in 8% to 22% of patients because of adverse reactions

Indication-Specific Adverse Events

- In first-line metastatic colorectal cancer (mCRC), the most common grade 3-4 events in Study 2107, which occurred at a ($\geq 2\%$) higher incidence in the bevacizumab plus IFL vs IFL groups, were asthenia (10% vs 7%), abdominal pain (8% vs 5%), pain (8% vs 5%), hypertension (12% vs 2%), deep vein thrombosis (9% vs 5%), intra-abdominal thrombosis (3% vs 1%), syncope (3% vs 1%), diarrhea (34% vs 25%), constipation (4% vs 2%), leukopenia (37% vs 31%), and neutropenia (21% vs 14%)
- In second-line mCRC, the most common grade 3-5 (nonhematologic) and 4-5 (hematologic) events in Study E3200, which occurred at a higher incidence ($\geq 2\%$) in the bevacizumab plus FOLFOX4 vs FOLFOX4 groups, were fatigue (19% vs 13%), diarrhea (18% vs 13%), sensory neuropathy (17% vs 9%), nausea (12% vs 5%), vomiting (11% vs 4%), dehydration (10% vs 5%), hypertension (9% vs 2%), abdominal pain (8% vs 5%), hemorrhage (5% vs 1%), other neurological (5% vs 3%), ileus (4% vs 1%), and headache (3% vs 0%). These data are likely to underestimate the true adverse event rates due to the reporting mechanisms used in this study

Continued on the next page

Please see full [Prescribing Information for ZIRABEV](#).

IMPORTANT SAFETY INFORMATION (Continued)

Indication-Specific Adverse Events

- In non-small cell lung cancer (NSCLC), grade 3-5 (nonhematologic) and grade 4-5 (hematologic) adverse events in Study E4599 occurring at a ($\geq 2\%$) higher incidence in bevacizumab-treated patients vs controls were neutropenia (27% vs 17%), fatigue (16% vs 13%), hypertension (8% vs 0.7%), infection without neutropenia (7% vs 3%), venous thromboembolism (5% vs 3%), febrile neutropenia (5% vs 2%), pneumonitis/pulmonary infiltrates (5% vs 3%), infection with grade 3 or 4 neutropenia (4% vs 2%), hyponatremia (4% vs 1%), headache (3% vs 1%), and proteinuria (3% vs 0%)
- In recurrent glioblastoma (rGBM) Study EORTC 26101, 22% of patients discontinued treatment in the bevacizumab with lomustine arm due to adverse reactions compared with 10% of patients in the lomustine arm. In patients receiving bevacizumab with lomustine, the adverse reaction profile was similar to that observed in other approved indications
- In metastatic renal cell carcinoma (mRCC), the most common grade 3-5 adverse events in Study BO17705, occurring at a ($\geq 2\%$) higher incidence in bevacizumab-treated patients vs controls, were fatigue (13% vs 8%), asthenia (10% vs 7%), proteinuria (7% vs 0%), hypertension (6% vs 1%, including hypertension and hypertensive crisis), and hemorrhage (3% vs 0.3%, including epistaxis, small intestinal hemorrhage, aneurysm ruptured, gastric ulcer hemorrhage, gingival bleeding, hemoptysis, hemorrhage intracranial, large intestinal hemorrhage, respiratory tract hemorrhage, and traumatic hematoma)
- In persistent, recurrent, or metastatic cervical cancer, grade 3 or 4 adverse reactions in Study GOG-0240, occurring at a higher incidence ($\geq 2\%$) in 218 patients receiving bevacizumab plus chemotherapy compared to 222 patients receiving chemotherapy alone, were abdominal pain (12% vs 10%), diarrhea (6% vs 3%), anal fistula (4% vs 0%), proctalgia (3% vs 0%), urinary tract infection (8% vs 6%), cellulitis (3% vs 0.5%), fatigue (14% vs 10%), hypertension (11% vs 0.5%), thrombosis (8% vs 3%), hypokalemia (7% vs 4%), hyponatremia (4% vs 1%), dehydration (4% vs 0.5%), neutropenia (8% vs 4%), lymphopenia (6% vs 3%), back pain (6% vs 3%), and pelvic pain (6% vs 1%)
- In stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer after primary surgery:
 - 608 patients received carboplatin and paclitaxel plus bevacizumab followed by bevacizumab (CPB15+), 607 patients received carboplatin and paclitaxel plus bevacizumab followed by placebo (CPB15), and 602 patients received carboplatin and paclitaxel plus placebo followed by placebo (CPP)
 - Grade 3-4 adverse reactions occurring at a higher incidence ($\geq 2\%$) in either of the bevacizumab arms vs the chemotherapy-only arm were fatigue (CPB15+, 9%; CPB15, 6%; CPP, 6%), hypertension (CPB15+, 10%; CPB15, 6%; CPP, 2%), thrombocytopenia (CPB15+, 21%; CPB15, 20%; CPP, 15%), and leukopenia (CPB15+, 51%; CPB15, 53%; CPP, 50%)
- In platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer (psOC), grade 3-4 adverse reactions in Study AVF4095g, occurring at a higher incidence ($\geq 2\%$) in 247 patients receiving bevacizumab plus carboplatin and gemcitabine (chemotherapy) compared to 233 patients receiving placebo plus chemotherapy, were thrombocytopenia (40% vs 34%), nausea (4% vs 1.3%), fatigue (6% vs 4%), headache (4% vs 0.9%), proteinuria (10% vs 0.4%), dyspnea (4% vs 1.7%), epistaxis (5% vs 0.4%), and hypertension (17% vs 0.9%)
- In platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, grade 3-4 adverse reactions in Study GOG-0213, occurring at a higher incidence ($\geq 2\%$) in 325 patients receiving bevacizumab plus carboplatin and paclitaxel (chemotherapy) compared to 332 patients receiving chemotherapy alone, were hypertension (11% vs 0.6%), fatigue (8% vs 3%), febrile neutropenia (6% vs 3%), proteinuria (8% vs 0%), abdominal pain (6% vs 0.9%), hyponatremia (4% vs 0.9%), headache (3% vs 0.9%), and pain in extremity (3.0% vs 0%)
- In platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer (prOC), grade 3-4 adverse reactions in Study MO22224, occurring at a higher incidence ($\geq 2\%$) in 179 patients receiving bevacizumab plus chemotherapy compared to 181 patients receiving chemotherapy alone, were hypertension (6.7% vs 1.1%) and palmar-plantar erythrodysesthesia syndrome (4.5% vs 1.7%)

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INDICATIONS

Metastatic Colorectal Cancer

ZIRABEV, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer (mCRC).

ZIRABEV, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with mCRC who have progressed on a first-line bevacizumab product-containing regimen.

Limitation of Use: ZIRABEV is not indicated for adjuvant treatment of colon cancer.

First-Line Non-Squamous Non-Small Cell Lung Cancer

ZIRABEV, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC).

Recurrent Glioblastoma

ZIRABEV is indicated for the treatment of recurrent glioblastoma (GBM) in adults.

Metastatic Renal Cell Carcinoma

ZIRABEV, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma (mRCC).

Persistent, Recurrent, or Metastatic Cervical Cancer

ZIRABEV, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.

Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

ZIRABEV, in combination with carboplatin and paclitaxel, followed by ZIRABEV as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.

ZIRABEV, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.

ZIRABEV, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by ZIRABEV as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

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