SELECTED 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

FDA-approved biosimilars such as bevacizumab-bvzr (ZIRABEV®) are recommended as treatment options in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[1-5*†]

INJECTION
Zirabev®
bevacizumab-bvzr
Pfizer

A PFIZER BIOSIMILAR BUILT ON EXPERIENCE

Part of the largest oncology biosimilars portfolio[6]

ZIRABEV product and reimbursement information for your practice

- Indications
- Pfizer Oncology Together™
- Payer Coverage by Region
- Important Safety Information
- Ordering
- References

Learn more about ZIRABEV

*Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar and the reference product.

†NCCN Guidelines® recommend the use of an FDA-approved biosimilar as an appropriate substitute for bevacizumab. See the NCCN Guidelines for detailed recommendations, including specific treatment regimens. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

ZIRABEV® (bevacizumab-bvzr) Is FDA Approved for the Following Eligible Indications of Avastin® (bevacizumab)[5]

INDICATIONS

Metastatic Colorectal Cancer (mCRC)

ZIRABEV, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with 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 (NSCLC)

ZIRABEV, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic NSCLC.

Recurrent Glioblastoma (GBM)

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

Metastatic Renal Cell Carcinoma (mRCC)

ZIRABEV, in combination with interferon alfa, is indicated for the treatment of mRCC.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

- **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 (≥1/2 tsp of red blood). Discontinue ZIRABEV in patients who develop grade 3-4 hemorrhage

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

ZIRABEV® (bevacizumab-bvzr) Is FDA Approved for the Following Eligible Indications of Avastin® (bevacizumab)(continued)[5]

INDICATIONS

Persistent, Recurrent, or Metastatic Cervical Cancer (CC)

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

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 stage III or IV disease following initial surgical resection.

ZIRABEV, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for platinum-resistant recurrent disease in patients who received no more than 2 prior chemotherapy regimens.

ZIRABEV, in combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by ZIRABEV as a single agent, is indicated for the treatment of platinum-sensitive recurrent disease.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

- 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%)

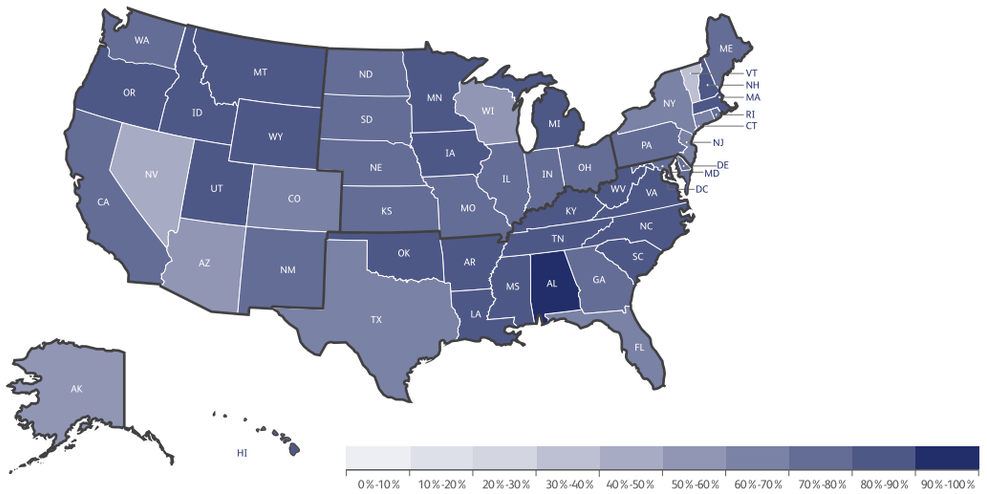
Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

ZIRABEV® (bevacizumab-bvzr) Payer Coverage†*

National and State Coverage Rates[7]

Individual state rates represent the percentage of commercial lives where ZIRABEV® (bevacizumab-bvzr) is covered at parity or at an advantage to Avastin® (bevacizumab)*†

Click on a region to learn more



National access rates at **parity** or **better**, compared to Avastin

73%
of commercially insured patients have access to ZIRABEV nationwide*†

93%
of Medicare lives covered nationwide, including managed Medicare*†

*As of April 2022.

†The information provided in this communication is not a guarantee of coverage or payment (partial or full). Actual benefits are determined by each plan administrator in accordance with its respective policy and procedures. Nothing herein may be construed as an endorsement, approval, recommendation, representation, or warranty of any kind by any plan or insurer.

SELECTED SAFETY INFORMATION

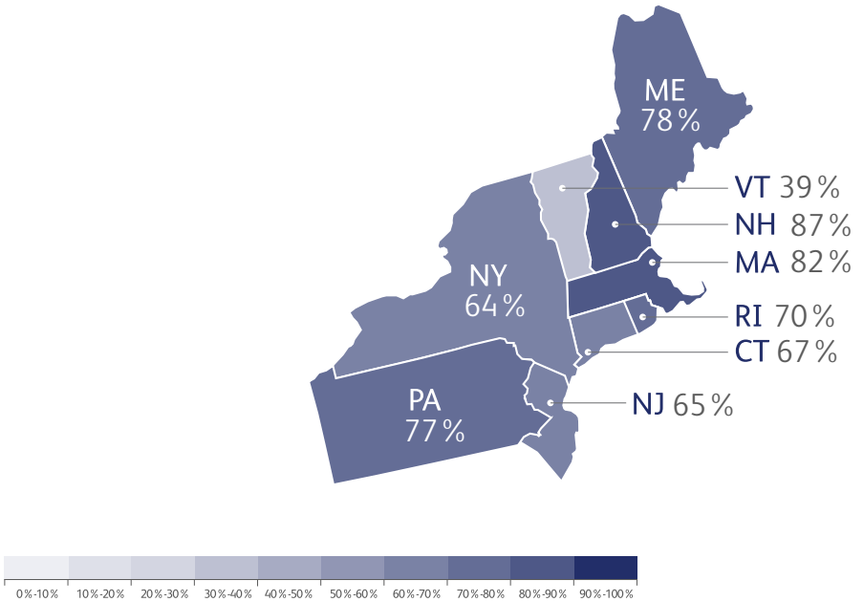
Warnings and Precautions (continued)

- 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

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

ZIRABEV® (bevacizumab-bvzr) *Payer Coverage**†

Northeastern United States



Individual state rates represent the percentage of commercial lives where ZIRABEV® (bevacizumab-bvzr) is covered at parity or at an advantage to Avastin® (bevacizumab)*†

*As of April 2022.

†The information provided in this communication is not a guarantee of coverage or payment (partial or full). Actual benefits are determined by each plan administrator in accordance with its respective policy and procedures. Nothing herein may be construed as an endorsement, approval, recommendation, representation, or warranty of any kind by any plan or insurer.

warranty of any kind by any plan or insurer.

SELECTED SAFETY INFORMATION

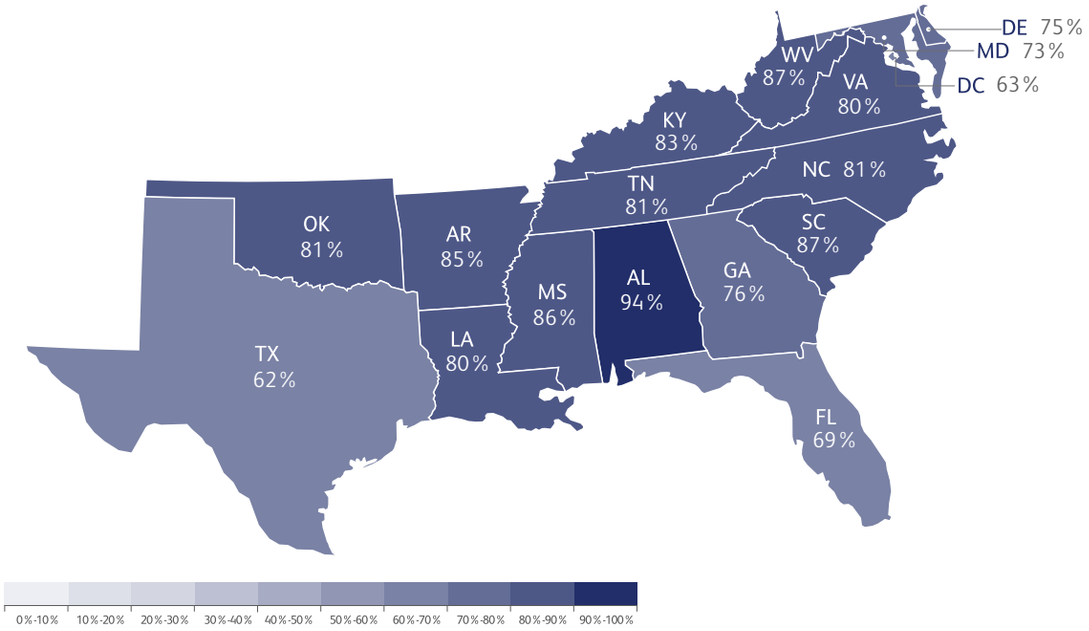
Warnings and Precautions (continued)

- 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

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

ZIRABEV® (bevacizumab-bvzr) *Payer Coverage**†

Southern United States



Individual state rates represent the percentage of commercial lives where ZIRABEV® (bevacizumab-bvzr) is covered at parity or at an advantage to Avastin® (bevacizumab)*†

*As of April 2022.

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warranty of any kind by any plan or insurer.

SELECTED SAFETY INFORMATION

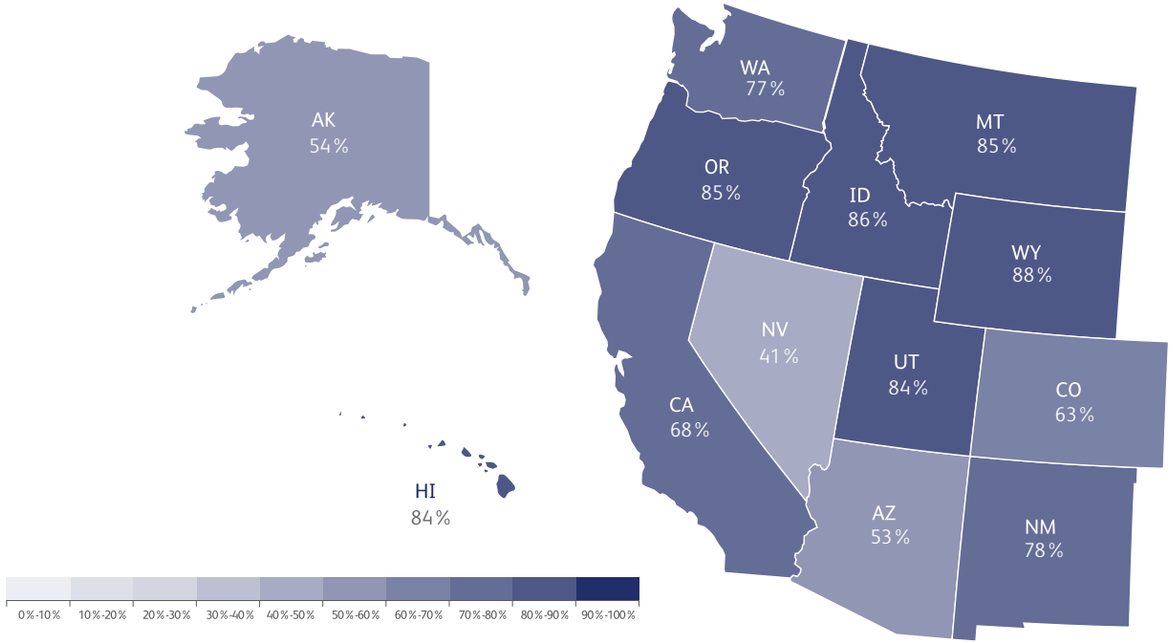
Warnings and Precautions (continued)

- 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

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

ZIRABEV® (bevacizumab-bvzr) *Payer Coverage**†

Western United States



Individual state rates represent the percentage of commercial lives where ZIRABEV® (bevacizumab-bvzr) is covered at parity or at an advantage to Avastin® (bevacizumab)*†

*As of April 2022.

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warranty of any kind by any plan or insurer.

SELECTED SAFETY INFORMATION

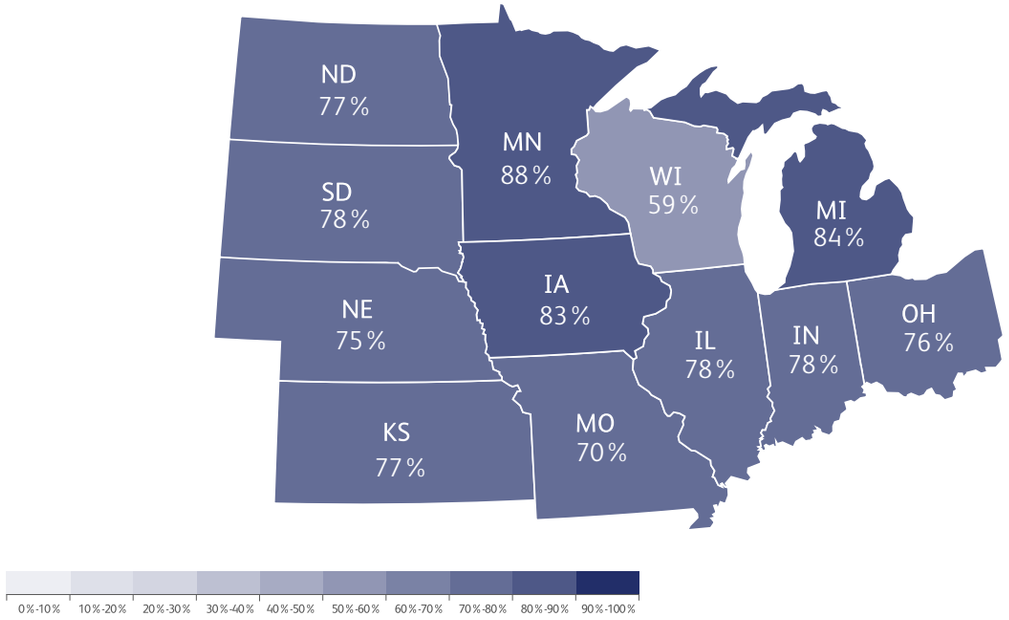
Warnings and Precautions (continued)

- 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

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

ZIRABEV® (bevacizumab-bvzr) *Payer Coverage**†

Midwestern United States



Individual state rates represent the percentage of commercial lives where ZIRABEV® (bevacizumab-bvzr) is covered at parity or at an advantage to Avastin® (bevacizumab)*†

*As of April 2022.

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warranty of any kind by any plan or insurer.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

- 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

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

An FDA-Approved Biosimilar to Avastin® (bevacizumab)[5]

ZIRABEV is available in single-dose vials for intravenous infusion[5]

Ordering ZIRABEV—What you need to know[5,7-9]

Unit of Sale	100 mg/4 mL SDV	400 mg/16 mL SDV
Unit of Sale NDC	0069-0315-01	0069-0342-01
Unit of Sale Quantity	1 vial per carton	1 vial per carton
Unit of Sale List Price*	$613.40	$2,453.60
HCPCS Code	Q5118	
OPPS Status	G: Pass-through payment	

OPPS=Outpatient Prospective Payment System; SDV=single-dose vial.
*As of May 2022.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

- **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

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

Pfizer Oncology together™

Making your patients' support needs a priority. Together.

Pfizer Oncology Together™ is a personalized support program to help patients and their loved ones throughout ZIRABEV treatment. We can assist with the access and reimbursement process and help identify financial assistance options for your patients prescribed ZIRABEV. And when your patients need support for their day-to-day challenges, we can provide them with a dedicated Care Champion who has social work experience and can connect them to resources that may help. Because when it comes to support, we're in this together.

FOR LIVE, PERSONALIZED SUPPORT
Call **1-877-744-5675** (Monday–Friday 8 AM–8 PM ET)

VISIT
PfizerOncologyTogether.com

SELECTED SAFETY INFORMATION

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

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

Important Safety Information and Indications

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 (≥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

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Important Safety Information and Indications (continued)

- **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 (≥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 (≥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

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Important Safety Information and Indications (continued)

- In non-small cell lung cancer (NSCLC), grade 3-5 (nonhematologic) and grade 4-5 (hematologic) adverse events in Study E4599 occurring at a (≥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 (≥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 (≥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 (≥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 (≥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 (≥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%)

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Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

Important Safety Information and Indications (continued)

- 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 (≥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 erythrodysaesthesia syndrome (4.5% vs 1.7%)

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.

Please see Important Safety Information and Indications on pages 7-10 and full Prescribing Information available at ZirabevHCP.com.

References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.5.2021. © 2021 National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the guideline, go online to NCCN.org.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer V.2.2021. © 2021 National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the guideline, go online to NCCN.org.
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