ZIRABEV®▼(bevacizumab) 25 mg/ml concentrate for solution for infusion

PRESCRIBING INFORMATION - IE

Please refer to the full Summary of Product Characteristics (SmPC) before prescribing Zirabev.

Presentation: Each 4 ml and 16 ml vial containing 100 mg or 400 mg respectively of bevacizumab concentrate for solution for infusion (bevacizumab is a recombinant humanised monoclonal antibody produced by DNA technology in Chinese Hamster Ovary cells). **Administration:** Intravenous (IV) infusion only under the supervision of a physician experienced in the use of antineoplastic medicinal products. If first (over 90 mins) and second (over 60 mins) infusions are well tolerated, all subsequent infusions may be administered over 30 mins. Dose reductions not recommended. If indicated, therapy should be stopped or temporarily suspended. **Indications and dosage:** 1) Zirabev (*5 or 10 mg/kg every 2 weeks or 7.5 or 15 mg/kg every 3 weeks*) in combination with fluoropyrimidine-based chemotherapy is indicated for treatment of adult patients with metastatic carcinoma of the colon or rectum. 2) Zirabev (*10mg/kg every 2 weeks or 15mg/kg every 3 weeks*) in combination with paclitaxel is indicated for first-line treatment of adult patients with metastatic breast cancer. 3) Zirabev in combination with capecitabine is indicated for first-line treatment of adult patients with metastatic breast cancer in whom treatment with other chemotherapy options including taxanes or anthracyclines is not considered appropriate. Patients who have received taxane and anthracycline-containing regimens in the adjuvant setting within the last 12 months should be excluded from treatment with Zirabev in combination with capecitabine. 4) Zirabev (*7.5 or 15 mg/kg every 3 weeks*), in addition to platinum-based chemotherapy *(for up to 6 cycles, then Zirabev monotherapy*), is indicated for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer other than predominantly squamous cell histology. 5) Zirabev (*15 mg/kg every 3 weeks*) in combination with erlotinib is indicated for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-squamous non-small cell lung cancer with Epidermal Growth Factor Receptor (EGFR) activating mutations. 6) Zirabev (*10 mg/kg every 2 weeks*) in combination with interferon alfa-2a is indicated for first line treatment of adult patients with advanced and/or metastatic renal cell cancer. 7) Zirabev (*15 mg/kg every 3 weeks*), in combination with carboplatin and paclitaxel (*for up to 6 cycles followed by Zirabev monotherapy until disease progression, a maximum of 15 months or until unacceptable toxicity, whichever occurs earlier*) is indicated for the front-line treatment of adult patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) stages III B, III C and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer. 8) Zirabev (*15 mg/kg every 3 weeks*), in combination with carboplatin and gemcitabine (*6 to 10 cycles, followed by Zirabev monotherapy*) or in combination with carboplatin and paclitaxel (*6 to 8 cycles, followed by Zirabev monotherapy*), is indicated for treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor–targeted agents. 9) Zirabev (*10 mg/kg every 2 weeks*) in combination with paclitaxel, topotecan (*given weekly*), or pegylated liposomal doxorubicin is indicated for the treatment of adult patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than two prior chemotherapy regimens and who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor–targeted agents. If topotecan is administered every 3 weeks, the Zirabev dose is 15 mg/kg every 3 weeks. 10) Zirabev (*15 mg/kg every 3 weeks*), in combination with paclitaxel and cisplatin or, alternatively, paclitaxel and topotecan in patients who cannot receive platinum therapy, is indicated for the treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix. **Elderly patients (≥ 65 years of age):** Dosage adjustments are not required in elderly patients. **Hepatic impairment & renal impairment:** The safety and efficacy have not been studied in patients with hepatic or renal impairment. **Paediatric patients (< 18 years):** Not indicated. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients. Hypersensitivity to Chinese Hamster Ovary (CHO) cell products or other recombinant human or humanised antibodies. Pregnancy. **Pregnancy and lactation:** Women of childbearing potential have to use effective contraception during (and up to 6 months after) treatment. Bevacizumab is contraindicated in pregnancy. Women must discontinue breast-feeding during therapy and not breast-feed for at least six months following the last dose of bevacizumab. **Warnings and precautions:** *Traceability:* Zirabev is a biological medicine; clearly record the name and batch number. There is an increased risk of developing the following serious conditions (see SmPC for full guidance on patient risk factors and when to discontinue or withhold Zirabev): Gastrointestinal (GI) perforations and fistulae, GI-vaginal fistulae, Non-GI fistulae, wound healing complications, hypertension, aneurysms and artery dissections, posterior reversible encephalopathy syndrome (PRES), proteinuria, arterial thromboembolism, venous thromboembolism, haemorrhage, pulmonary haemorrhage/haemoptysis, congestive heart failure, neutropenia and infections, hypersensitivity reactions/infusion reactions, osteonecrosis of the jaw. Zirabev is not formulated for intravitreal use. Unapproved intravitreal use has led to serious ocular adverse reactions including permanent blindness as well as systemic adverse effects including non-ocular haemorrhages and arterial thromboembolic reactions. As bevacizumab may cause ovarian failure, discuss fertility preservation strategies with women of child-bearing potential prior to starting treatment. Consideration should be given to patients who are on a controlled sodium diet. *Sodium content*: 3 mg sodium per 4 ml vial and 12.1 mg sodium per 16 ml vial.

Side-effects: The overall safety profile of bevacizumab is based on data from over 5,700 patients with various malignancies, predominantly treated with bevacizumab in combination with chemotherapy in clinical trials. The most serious adverse reactions were: gastrointestinal perforations; haemorrhage, including pulmonary haemorrhage/haemoptysis, which is more common in non-small cell lung cancer patients: arterial thromboembolism. The most frequently observed adverse reactions across clinical trials in patients receiving bevacizumab were hypertension, fatigue or asthenia, diarrhoea and abdominal pain. Very common (≥ 1/10) side effects were: febrile neutropenia, leucopenia, neutropenia, thrombocytopenia, anorexia, hypomagnesaemia, hyponatraemia, peripheral sensory neuropathy, dysarthria, headache, dysgeusia, eye disorder, lacrimation increased, hypertension, thrombo-embolism (venous), dyspnoea, rhinitis, epistaxis, cough, rectal haemorrhage, stomatitis, constipation, diarrhoea, nausea, vomiting, abdominal pain, wound healing complications, exfoliative dermatitis, dry skin, skin discoloration, arthralgia, myalgia, proteinuria, ovarian failure, asthenia, fatigue, pyrexia, pain, mucosal inflammation, weight decreased.

Common (≥1/100 to <1/10) reported side-effects were: sepsis, abscess, cellulitis, infection, urinary tract infection, anaemia, lymphopenia, hypersensitivity, infusion reactions, dehydration, cerebrovascular accident, syncope, somnolence, congestive heart failure, supraventricular tachycardia, thrombo-embolism (arterial), haemorrhage, deep vein thrombosis, pulmonary haemorrhage/haemoptysis, pulmonary embolism, hypoxia, dysphonia, gastrointestinal perforation, intestinal perforation, ileus, intestinal obstruction, recto-vaginal fistulae, gastrointestinal disorder, proctalgia, palmar-plantar erythro-dysaesthesia syndrome, fistula, muscular weakness, back pain, pelvic pain and lethargy. The following severe side effects (frequency not known) have also been reported: necrotising fasciitis, hypersensitivity, infusion reactions, posterior reversible encephalopathy syndrome, hypertensive encephalopathy, aneurysms and artery dissections, renal thrombotic microangiopathy, pulmonary hypertension, nasal septum perforation, GI ulcer and perforation, rectal haemorrhage, gallbladder perforation, osteonecrosis of the jaw, non-mandibular osteonecrosis, ovarian failure, foetal abnormalities. See SmPC for full details on all other side effects. **Driving and operating machinery:** If patients are experiencing symptoms that affect their vision or concentration, or their ability to react, they should be advised not to drive and use machines until symptoms abate. **Legal category:** POM, S1A **Marketing Authorisation Number:** EU/1/18/1344/001, EU/1/18/1344/002 **Marketing Authorisation Holder:** Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.

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Ref: bZR 6_0

For further information on this medicine please contact: Pfizer Medical Information on 1800 633 363 or at medical.information@pfizer.com. For queries regarding product availability please contact: Pfizer Healthcare Ireland, Pfizer Building 9, Riverwalk, National Digital Park, Citywest Business Campus, Dublin 24 + 353 1 4676500.

References

1. Pfizer ZIRABEV® (bevacizumab) Summary of Product Characteristics.
2. Pfizer Cisplatin Summary of Product Characteristics.

For more information or in case of specific medical questions, please contact **Pfizer Medical information**.

Email: EUMEDINFO@pfizer.com

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Pfizer Oncology

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Zirabev®
bevacizumab

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DOSING GUIDELINES

ZIRABEV®▼ – BUILDING ONTO THE EXPERIENCE OF BEVACIZUMAB WITH PFIZER[1]

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Refer to section 4.8 of the SPC for how to report adverse reactions.

Zirabev®▼
bevacizumab

INDICATIONS AND DOSING[1,2]

ZIRABEV® (bevacizumab) has the same dosing as the reference Bevacizumab.

INDICATION		COMBINATION	DOSING
	**METASTATIC CARCINOMA OF THE COLON OR RECTUM (mCRC)**	With fluoropyrimidine-based chemotherapy	5 mg/kg or 10 mg/kg once every 2 weeks or 7.5 mg/kg or 15 mg/kg once every 3 weeks
	**UNRESECTABLE ADVANCED, METASTATIC OR RECURRENT NON-SMALL CELL LUNG CANCER OTHER THAN PREDOMINANTLY SQUAMOUS CELL HISTOLOGY**	With platinum-based chemotherapy for first-line treatment	7.5 mg/kg or 15 mg/kg once every 3 weeks
	NON-SQUAMOUS NON-SMALL CELL LUNG CANCER (NSCLC) WITH EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) ACTIVATING MUTATIONS	With erlotinib for first-line treatment	15 mg/kg of body weight given once every 3 weeks
	**METASTATIC BREAST CANCER**	With paclitaxel for first-line treatment	10 mg/kg once every 2 weeks or 15 mg/kg once every 3 weeks
		With capecitabine for first-line treatment	
	**ADVANCED AND/OR METASTATIC RENAL CELL CANCER**	With interferon alfa-2a	10 mg/kg once every 2 weeks
	**CERVICAL CANCER - PERSISTENT, RECURRENT OR METASTATIC CARCINOMA**	With paclitaxel and cisplatin, or paclitaxel and topotecan	15 mg/kg once every 3 weeks
	**EPITHELIAL OVARIAN, FALLOPIAN TUBE OR PRIMARY PERITONEAL CANCER** — Front-line treatment	With carboplatin and paclitaxel	15 mg/kg once every 3 weeks
	First recurrence platinum sensitive	With carboplatin and gemcitabine or carboplatin and paclitaxel	15 mg/kg once every 3 weeks
	First recurrence platinum resistant	With paclitaxel, topotecan, or pegylated liposomal doxorubicin	10mg/kg once every 2 weeks with Paclitaxel and Pegylated liposomal doxorubicin. 15mg/kg once every 3 weeks with Topotecan

CONTRAINDICATIONS:[1]

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SmPC.
- Hypersensitivity to Chinese Hamster Ovary (CHO) cell products or other recombinant human or humanised antibodies.
- Pregnancy (see section 4.6 of the SmPC).

STABILITY DATA[1]

STABILITY DATA			
	Unopened Vial (Refrigerated)	3 years	In a refrigerator: 2°C-8°C
	Post-dilution*	35 days	2°C-8°C
		48 hours	2°C-30°C

* Chemical and physical in-use stability has been demonstrated for a period of up to 35 days at 2°C to 8°C after dilution and a period of up to 48 hours at temperatures not exceeding 30°C in sodium chloride 9 mg/ml (0.9%) solution for injection. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

STORAGE[1]

Store in a refrigerator (2° - 8°)

Do not freeze

Keep the vial in the outer carton in order to protect from light.

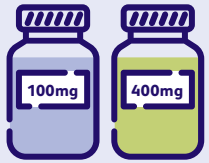
ADMINISTRATION[1]

ZIRABEV® is for intravenous use. The initial dose should be delivered over 90 minutes as an intravenous infusion. If the first infusion is well tolerated, the second infusion may be administered over 60 minutes. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 minutes. It should not be administered as an intravenous push or bolus. Dose reduction for adverse reactions is not recommended.
If indicated, therapy should either be permanently discontinued or temporarily suspended as described in section 4.4 of ZIRABEV® SmPC.

DISPOSAL AND HANDLING[1]

ZIRABEV® should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared solution. Once the vial has been opened, the dilution must be performed immediately. The necessary amount of bevacizumab should be withdrawn and diluted to the required administration volume with sodium chloride 9 mg/ml (0.9%) solution for injection. The concentration of the final bevacizumab solution should be kept within the range of 1.4 mg/ml to 16.5 mg/ml. In the majority of the occasions the necessary amount of ZIRABEV® can be diluted with 0.9% sodium chloride solution for injection to a total volume of 100 mL. Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. ZIRABEV® is for single-use only, as the product contains no preservatives. Any unused medicinal product or waste material should be disposed in accordance with local requirements.

NATURE AND CONTENT OF CONTAINER[1]



4 ml solution in a vial (Type I glass) with a stopper (butyl rubber) containing 100 mg of bevacizumab. 16 ml solution in a vial (Type I glass) with a stopper (butyl rubber) containing 400 mg of bevacizumab.

Zirabev®
bevacizumab