Abarelix (Plenaxis™)

William P. Hogle, RN, BSN, OCN®

Drug name: Abarelix is marketed under the trade name Plenaxis™ (Praecis Pharmaceuticals Inc., Waltham, MA).

Classification: Gonadotropin-releasing hormone (GNRH) antagonist.

Action: GNRH, also known as leutinizing hormone-releasing hormone (LHRH), binds to the anterior pituitary gonadotropic cells and stimulates the secretion of leutinizing hormone (LH) and follicle stimulating hormone (FSH). Once LH and FSH enter the circulatory system, they act on the testes, causing them to produce testosterone and dihydrotosterone (DHT), both of which are considered androgens. LH and FSH are needed for the prostate gland to function normally and also have a role in the sustenance of malignant prostate tissue. Abarelix inhibits GNRH from binding to gonado tropic cells, thus preventing the secretion of LH and FSH. The cascade of hormone secretion is interrupted at a very early stage, preventing the production of significant levels of the male hormones testosterone and DHT, which are known to lead to the proliferation of androgen-dependent and androgen-sensitive prostate cancer cells. Unlike currently available LHRH agonists, abarelix does not induce an initial surge of testosterone or other known androgens.

Indications: Abarelix currently is indicated for the palliative treatment of men with advanced symptomatic prostate cancer in whom LHRH agonist therapy is not appropriate or who refuse surgical castration and meet at least one of the following criteria.

- Risk of neurologic complications resulting from metastatic disease
- Obstruction of the ureters or outlet of the urinary bladder because of localized encroachment or metastatic disease
- High levels of bone pain from skeletal metastases despite ongoing use of narcotic analgesia

As with the administration of any hormonal agent for the treatment of prostate cancer, abarelix is not intended to be curative. It can, however, provide patients with symptomatic relief from the complications listed previously and palliation.

Metabolism: Studies have indicated that abarelix is metabolized in the liver without evidence of cytochrome p 450 involvement.

Excretion: No detectable metabolites were found in the urine. Approximately 13% of unmetabolized abarelix was found in urine after a 15 mcg/kg intramuscular (IM) injection. Renal clearance of abarelix was 14.4 L per day (10 ml per minute) following administration of 100 mg of the drug.

Absorption: After IM administration of 100 mg of abarelix, absorption peaked with a concentration level of 43.4 ng/ml observed approximately three days following injection.

Effect on blood counts: No evidence suggests that abarelix has a significant effect on bone marrow production.

Adverse reactions and events: The most significant adverse event associated with the administration of abarelix is an immediate onset systemic allergic reaction most often occurring within eight minutes of administration. The exact nature of the reported allergic reactions remains unclear. Phase IV clinical studies are under way to make this determination. The incidence rate of this type of severe allergic reaction was reported in 3.7% of patients with advanced symptomatic prostate cancer and 1.1% of all patients with prostate cancer. These immediate onset reactions have been reported to occur following any administration of abarelix, including the initial dose. The cumulative risk of such a reaction increases with the duration of treatment. Other adverse reactions to abarelix that have occurred with increased frequency include heat flashes (79%), sleep disturbance (44%), pain (31%), breast enlargement (30%), breast or nipple tenderness (20%), back pain (17%), constipation (15%), peripheral edema (15%), dizziness (12%), headache (12%), upper respiratory infection (URI) (12%), and diarrhea (11%).

Approximately 20% of patients who received abarelix in clinical trials experienced prolonged QT interval changes on electrocardiograms. Whether this was a direct result of drug administration, androgen deprivation therapy, or other unknown variables has not been determined.

Patients also were found to have elevated serum transaminase levels of alanine aminotransferase (ALT) and aspartate transaminase (AST). Two different studies demonstrated elevated serum ALT levels that were more than 2.5 times the upper levels of normal in 8.2% and 1.8% of patients, respectively, and serum AST levels more than 2.5 times the upper levels of normal in 3.1% and 0.8% of patients, respectively.

As with most GNRH antagonists, a decrease in bone mineral density is possible and should be taken into consideration. Further, because patients can become refractory to abarelix, they should have their serum testosterone levels monitored periodically.

Route and dosage: The recommended dosage of abarelix is 100 mg administered as an IM injection into the buttock on days 1, 15, 29, and every four weeks thereafter. Because of the possibility of a localized skin reaction, injection sites in the right and left buttocks should be alternated with each subsequent injection.

Dilution and reconstitution: Abarelix is supplied as a single-dose, preservative-free, sterile powder that, when reconstituted with...
Abarelix (Plenaxis™) Patient Instruction Sheet

**Action:** Abarelix is known as a gonadotropin-releasing hormone (GNRH). The drug lowers the levels of testosterone in the blood by blocking cells in the body from receiving the necessary hormones required for testosterone production.

**How is the drug given?** Abarelix can be prescribed only by physicians who are part of the Plenaxis™ PLUS Program. Physicians must receive specialized instruction from the manufacturer before prescribing this drug. Abarelix is administered as an injection into the buttocks. The drug typically is prescribed once every two weeks for the first month and then every four weeks thereafter.

**Why am I receiving this drug?** Abarelix is used in the treatment of advanced prostate cancer. Patients who refuse other forms of treatment or cannot tolerate other medications used to treat prostate cancer may be candidates for abarelix. Patients must realize that abarelix is not a curative agent and is intended to provide symptomatic relief from advanced prostate cancer. If your doctor has prescribed abarelix for you, you probably are at risk for nerve injury or urinary obstruction from advanced prostate cancer or you may be experiencing high levels of bone pain from the spread of prostate cancer.

**Side effects:** Abarelix may cause a serious allergic or life-threatening reaction that may require emergency medical treatment. The chance of experiencing a life-threatening allergic reaction is low but may increase with each injection of abarelix. Side effects that may require emergent treatment include:
- Low blood pressure
- Fainting
- Swelling of the face, eyelids, tongue, or throat
- Asthma, wheezing, or other breathing problems, including shortness of breath or chest tightness
- Possible change in heart rhythm that can cause fainting or death.

Less emergent side effects include:
- Allergic skin reactions such as a rash, hives, itching, tingling, and redness, all of which can happen immediately after drug injection or several days later
- Changes in liver function that are not considered serious and usually go away when abarelix is discontinued
- Decreased bone mineral density (caused by extended treatment), which can lead to thinning of the bones (i.e., osteopenia) and osteoporosis.

The most common side effects include:
- Hot flashes
- Difficulty falling or staying asleep
- Back discomfort
- Breast enlargement or breast or nipple discomfort
- Constipation.

**Precautions:** Prior to starting treatment with abarelix, patients are given an instructional booklet and asked to sign an understanding form to ensure that proper education, risks, and side-effect disclosure has occurred. Because of a potential life-threatening allergic reaction after receiving abarelix, patients are advised to wait in the doctor’s office for 30 minutes after each injection. Patients should alert their doctors about any other medications that they are taking, including prescription and nonprescription medicines, vitamins, and herbal supplements. Abarelix has not been studied with other medications. Therefore, potential interactions with other drugs are unknown. Notify your doctor if you or a family member has a heart condition known as prolongation of the QT interval. Your doctor may order a number of tests before starting abarelix to have baseline information about your current health status. These may include an electrocardiogram, a bone density study, and blood tests that specifically look at liver function and testosterone levels as well as a prostate specific antigen level. These blood tests may be monitored periodically throughout your treatment course.

Abarelix may not be as effective for men weighing more than 225 pounds. Studies have yet to be performed on this patient population to determine the effectiveness and severity of side effects of abarelix.

**What should I report to the healthcare team?** The following should be reported immediately to your oncology healthcare practitioner:
- Fainting or blackout spells
- Swelling of the face or eyelids
- Difficulty chewing, swallowing, or speaking
- Shortness of breath or wheezing
- Rash, hives, itching, tingling, or redness at the injection site or anywhere else on the body
- Irregular heart palpitations

2.2 ml of 0.9% sodium chloride solution, yields a 2 ml dose of 100 mg (50 mg/ml) as a depot suspension.

**Interactions:** No formal drug-drug interaction studies with abarelix have been performed.

**Contraindications:** Abarelix is contraindicated in patients with a known hypersensitivity to the drug or any of its components. It is not indicated in women or pediatric patients. Precautions should be taken when administering to patients with electrocardiogram-documented prolonged QT intervals as well as those patients weighing more than 225 pounds. Patients in this weight category have not been adequately studied and followed for drug efficacy and side effects.

**Stability:** Abarelix is supplied as a preservative-free powder and should be administered within one hour after reconstitution.

**Premedications:** No premedications currently are indicated for abarelix. Pending the outcome of phase IV clinical studies aimed at determining the nature of the reported allergic reactions, premedications may be indicated in the future.

**Nursing implications:** Nurses caring for patients who are receiving abarelix should do the following:
- Ensure that the prescribing physician has taken part in the Plenaxis PLUS Program, which provides physicians with specialized prescribing instructions from the manufacturer.
- Ensure that patients have been given an instructional booklet about abarelix and have signed an understanding form to ensure that education, risk, and side effect disclosure has occurred.
- Obtain a comprehensive cardiac and allergy history from all patients.
- Inform patients that a serious systemic allergic reaction is possible with initial and subsequent injections.
- Monitor for serious or life-threatening reactions, such as hypotension, bronchospasm, or shortness of breath, cardiac palpitations, facial or periorbital edema, edematous tongue, or dysphagia for up to 30 minutes following injection.
- Be prepared to administer supportive measures in the event that a systemic allergic reaction associated with hypotension or syncope occurs (oxygen, IV fluids, antihistamines, corticosteroids, or epinephrine).
- Monitor for localized skin injection site reactions, such as hives, redness, or itching.
- Evaluate for less common side effects, such as constipation, peripheral edema,
dizziness, headache, URI, and diarrhea.
• Discuss methods that may be helpful in coping with hot flashes, such as decreasing caffeine intake, dressing in layered clothing, and wearing cotton underclothes.
• Discuss methods to help patients cope with sleep disturbances, such as participating in a physician-approved exercise program, planning uninterrupted time for sleep and rest periods, prioritizing and rearranging patient activities, and administering a nighttime sedative.
• Monitor serum transaminase and prostate specific antigen levels prior to administration of abarelix and periodically during treatment.
• Evaluate for possible treatment failure by monitoring serum testosterone levels prior to administration of abarelix and periodically during treatment.
• Evaluate patients on long-term therapy for signs and symptoms of osteopenia or osteoporosis.
• Refer patients to Praecis Pharmaceuticals’ patient assistance program if their prescription coverage or financial situation is a concern.

Patient education: Patients receiving abarelix should
• Be aware that a serious life-threatening event may occur with the initial or any subsequent administration of abarelix.
• Be instructed that the drug administration schedule should be as follows: IM injection on days 1, 15, 29, and every four weeks thereafter.
• Know that they will be expected to stay in the office setting for at least 30 minutes after the administration of abarelix.
• Be notified of the side-effect profile of abarelix and encouraged to report any such side effects to their oncology healthcare practitioner.
• Understand that abarelix is not a curative agent and is intended to provide symptomatic relief.

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Bibliography

Part 2 of Cancer Treatments appears on the following pages.
Bevacizumab (Avastin®)

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Drug name: Bevacizumab is manufactured as Avastin® (Genentech, Inc., South San Francisco, CA).

Classification: Humanized monoclonal antibody produced by recombinant DNA technology

Action: Bevacizumab binds vascular endothelial growth factor (VEGF) and prevents the interaction of VEGF to its receptors (Flt-1 and KDR) on the surface of endothelial cells.

The interaction of VEGF with its receptors leads to endothelial cell proliferation and new blood vessel formation in vitro models of angiogenesis. Bevacizumab binds to VEGF with high affinity, minimizing the amount of circulating VEGF available to bind to the receptors and activate the angiogenesis process (Genentech BioOncology, 2004; Muehlbauer, 2003).

Indications: Bevacizumab, used in combination with IV 5-fluorouracil (5-FU)-based chemotherapy, is indicated for first-line treatment of patients with metastatic carcinoma of the colon or rectum. The U.S. Food and Drug Administration (2004) approved bevacizumab based on data from a phase III, randomized, placebo-controlled clinical trial that demonstrated a prolongation in the median survival of patients treated with bevacizumab plus the irinotecan/5-FU/leucovorin (IFL) chemotherapy regimen by approximately five months, compared to patients treated with the IFL chemotherapy regimen alone (20.3 months versus 15.6 months, respectively) (Hurwitz et al., 2004). In addition, this study demonstrated an improvement in progression-free survival (PFS) of more than four months (10.6 months versus 6.4 months) (Hurwitz et al.). The survival and PFS results observed when bevacizumab was added to first-line chemotherapy are the longest ever reported in a randomized, phase III study of patients with metastatic colorectal cancer.

Metabolism and excretion: Bevacizumab is degraded by the reticuloendothelial system; clearance varied by body weight, gender, and tumor burden. In a randomized study of 813 patients, no evidence existed of lesser efficacy in males or patients with higher tumor burden (Hurwitz et al., 2004).

Half-life: The estimated half-life of bevacizumab is approximately 20 days; the predicted time to reach steady state is 100 days.

Effect on blood counts: The four most common grade 3 or 4 adverse events seen in the phase III clinical trial were leukopenia, neutropenia, diarrhea, and hypertension, with percentages for IFL plus bevacizumab versus IFL plus placebo as follows.

- Leukopenia: 37% versus 31%
- Diarrhea: 34% versus 25%
- Hypertension: 12% versus 2%
- Neutropenia: 21% versus 14%

The largest increase in grade 3 or 4 adverse events seen with IFL plus bevacizumab were hypertension and diarrhea, with hypertension being the only statistically significant grade 3 or 4 event (Hurwitz et al., 2004).

Adverse reactions and events: In a phase III trial of 813 patients, the most serious adverse events that occurred with bevacizumab included gastrointestinal (GI) perforation and wound healing complications (Hurwitz et al., 2004). Although rare, these are potentially life-threatening events and, as such, are listed in the black box warning of the prescribing information. Hemorrhage, manifested as serious or fatal hemoptysis, was seen in a small study of patients with non-small cell lung cancer (NSCLC) and also is included in the black box warnings. Bevacizumab therapy is not indicated for the treatment of NSCLC.

Bevacizumab should be discontinued permanently in patients who develop GI perforation, wound dehiscence requiring medical intervention, serious bleeding, nephritic syndrome, or hypertensive crisis.

- GI perforation and wound dehiscence, complicated by intra-abdominal abscesses, occurred at an increased incidence in patients receiving bevacizumab compared to controls.
- The incidence of GI perforation in the trial was 0.3% of patients (1 of 396) receiving IFL plus placebo, 2% (6 of 392) receiving IFL plus bevacizumab, and 4% (4 of 109) receiving 5-FU/leucovorin (LV) plus bevacizumab (Hurwitz et al., 2004). These episodes occurred with or without intra-abdominal abscess and at various time points during treatment. The typical presentation was reported as abdominal pain associated with symptoms such as constipation and vomiting.

- Bevacizumab has been shown to impair wound healing in preclinical animal models. In one trial (Hurwitz et al., 2004), wound dehiscence was seen in 0.5% of patients (2 of 396) receiving IFL plus placebo and 1% of patients receiving chemotherapy plus bevacizumab (4 of 396 receiving IFL plus bevacizumab and 1 of 109 patients receiving 5-FU/LV plus bevacizumab).

- Serious and, in some cases, fatal hemoptysis has occurred in patients with NSCLC treated with chemotherapy and bevacizumab. In a small study, the incidence of serious or fatal hemoptysis was 31% in patients with squamous histology and 4% in patients with adenocarcinoma receiving bevacizumab compared to no cases in patients treated with chemotherapy alone. Patients with recent hemoptysis should not receive bevacizumab (Genentech BioOncology, 2004). Other potential adverse events include the following.

- Two distinct patterns of bleeding have occurred in patients receiving bevacizumab. Minor bleeding, commonly grade 1 epistaxis (nosebleed), was reported in 35.3% of patients who received IFL plus bevacizumab compared to 10.2% of patients who received IFL alone (Hurwitz et al., 2004). Epistaxis generally lasted less than five minutes, resolved without medical intervention, was not noted to be
infusion related, and did not require any changes in bevacizumab therapy. Other mild to moderate hemorrhagic events reported more frequently in patients receiving IFL plus bevacizumab compared to IFL alone include GI hemorrhage (24% versus 6%), vaginal bleeding (4% versus 2%), and minor gum bleeding (2% versus 0%) (Hurwitz et al.).

- The incidence of hypertension and severe hypertension was increased in patients receiving bevacizumab. Sixty percent of patients receiving bevacizumab plus IFL and 67% of patients receiving bevacizumab plus 5-FU/LV experienced hypertension (higher than 150/100 mmHg) compared with 43% receiving IFL alone. Seven percent of patients receiving bevacizumab plus IFL and 10% of patients receiving bevacizumab plus 5-FU/LV experienced severe hypertension (higher than 200/110 mmHg) compared with 2% receiving IFL alone. Standard oral antihypertensives, including angiotensin-converting enzymes (ACE inhibitors), beta blockers, diuretics, and calcium channel blockers were used to manage hypertension (Hurwitz et al., 2004). Across all clinical studies, developing or worsening hypertension, including hypertensive crisis, resulting in hospitalization or discontinuation of therapy occurred in 17 of 1,032 patients (1.6%) (Hurwitz et al.).

- Thromboembolic events, which were not graded, were slightly increased in the phase III trial, occurring in 19.3% of bevacizumab-treated patients and 16.1% of patients who received chemotherapy plus placebo (Hurwitz et al., 2004). This difference was not statistically significant. Clinically significant thromboembolic events included pulmonary embolism, deep venous thrombosis, and mesenteric vein thrombosis. Whether the thromboembolic events were associated with the patients’ underlying cancer, their chemotherapy or bevacizumab treatment, or other causes could not be determined.

- Evidence suggests an increased risk of serious arterial thromboembolic events, including cerebrovascular accidents (stroke), myocardial infarctions, transient ischemic attacks, and angina related to the use of bevacizumab. The risk of fatal thrombotic events also is increased. Patients who experience an arterial thromboembolic event during treatment should permanently discontinue bevacizumab (Genentech BioOncology, 2004). In randomized, active-controlled studies conducted in patients with metastatic colorectal cancer, the risk of a serious arterial thrombotic event was approximately two-fold higher in patients receiving infusional 5-FU–based chemotherapy plus bevacizumab, with an estimated overall rate of up to 5%. Risk factors for the development of arterial thromboembolic events included a history of arterial thromboembolism prior to bevacizumab exposure, age 65 and older, and bevacizumab therapy. Such events occur at a higher rate in these high-risk groups (Genentech BioOncology).

- Both the incidence and severity of proteinuria (defined as a urine dipstick reading of 1+ or higher) were increased in patients receiving bevacizumab versus those receiving IFL alone in the phase III trial. Nephrotic syndrome occurred in 5 of 1,032 patients (0.5%) receiving bevacizumab across multiple tumor types and clinical trials (Hurwitz et al., 2004). Patients receiving bevacizumab should be monitored for the development or worsening of proteinuria by serial urinalysis. Patients with a 2+ or higher urine dipstick reading should undergo further assessment (e.g., a 24-hour urine collection). Patients with moderate to severe proteinuria based on 24-hour urine collection should be monitored regularly until improvement or resolution is observed. In most clinical trials, bevacizumab was interrupted if 24-hour urine collection was higher than 2 g every 24 hours and then resumed when proteinuria fell below 2 g every 24 hours (Genentech BioOncology, 2004).

Route and dosage: The recommended dosage of bevacizumab is 5 mg/kg given once every 14 days as an IV infusion following chemotherapy until disease progression is detected. The drug should not be administered as an IV push or bolus. No dose reductions are recommended.

Dilution and reconstitution: Bevacizumab is supplied in 100 mg and 400 mg preservative-free, single-use vials containing 4 mg and 16 mg, respectively (25 mg/ml). Bevacizumab is a clear to slightly opalescent, colorless to pale brown, sterile solution for IV infusion.

- Using aseptic technique, withdraw the necessary amount of bevacizumab and dilute in a total volume of 100 ml of 0.9% sodium chloride, USP.
- Do not administer or mix bevacizumab infusions with dextrose solutions.
- Discard any unused portion left in the vial because the product contains no preservative.

Interactions: No formal drug interaction studies with antineoplastic agents have been conducted. Bevacizumab is not compatible with dextrose solutions and should be diluted with 0.9% normal saline.

Contraindications: No known contraindications to the use of bevacizumab have been reported.

Stability:
- Bevacizumab vials must be refrigerated at 2°–8°C (36°–46°F) and should be protected from light. Store in the original carton.
- Do not freeze or shake.
- Diluted bevacizumab solutions for infusion may be stored at 2°–8°C (36°–46°F) for eight hours.

Rate: The initial dose of bevacizumab is administered for 90 minutes as a continuous IV infusion. If the first infusion is well tolerated, the second infusion may be administered for 60 minutes. If a patient experiences infusion-related adverse events during the 60-minute infusion, subsequent doses should be given over 90 minutes. If the 60-minute infusion is well tolerated, subsequent infusions may be infused over 30 minutes. If well tolerated, all subsequent doses can be infused over 30 minutes. If a patient experiences infusion-related adverse events at the 30-minute infusion rate, subsequent infusions should remain at the 60-minute infusion rate.

Precordinations: Infusion reactions with the first dose of bevacizumab were uncommon (less than 3%); therefore, no premedications are recommended prior to the infusion of bevacizumab. Bevacizumab infusion should be interrupted in all patients with severe infusion reactions, and appropriate medical therapy should be administered.

Nursing implications: Nurses caring for patients receiving bevacizumab should do the following.
- Complete a patient history and physical assessment.
- Use with caution in patients with known hypersensitivity to bevacizumab or any component of the drug product.
- Do not ignore the patient’s complaint of abdominal pain. GI perforation should be included in the differential diagnosis of patients presenting with abdominal pain with nausea, vomiting, or constipation.
- Bevacizumab therapy should not be initiated for at least 28 days following major surgery. The surgical incision should be fully healed prior to the initiation of bevacizumab. The appropriate interval between termination of bevacizumab and subsequent elective surgery has not been determined and should take into consideration the calculated half-life (approximately 20 days).
- Monitor vital signs, including blood pressure per clinic standards and at least every two to three weeks while on therapy.
Bevacizumab (Avastin®) Patient Instruction Sheet

**Drug:** Bevacizumab (generic name) is manufactured as Avastin® (trade name).

**Action:** Bevacizumab is the first of a new class of drugs designed to inhibit angiogenesis or new blood vessel formation. The U.S. Food and Drug Administration (FDA) approved the drug to treat cancer of the colon or rectum. Bevacizumab is not chemotherapy but is given in combination with chemotherapy. Whereas chemotherapy attacks the tumor directly, bevacizumab attacks the blood vessels surrounding the tumor (Genentech, Inc., 2004).

To grow and spread, tumors need a constant supply of oxygen and other nutrients. Tumors get this supply by creating their own network of blood vessels. This process is called angiogenesis. To start angiogenesis, a tumor sends out signals to nearby blood vessels. These signals cause new blood vessels to “spout” toward the tumor. Once these new vessels reach the tumor, they provide the supply of blood that “feeds” the tumor (Genentech, Inc., 2004; Muehlbauer, 2003).

Bevacizumab works by blocking angiogenesis. Because of this, it is often referred to as anti-angiogenic therapy. By preventing the growth of new blood vessels, bevacizumab helps to “starve” the tumor. This makes it hard for the tumor to grow. On average, people taking bevacizumab in combination with chemotherapy were more likely to live longer, have a longer period of time before their tumors grew, and have their tumors become smaller in size (Genentech BioOncology, 2004; Muehlbauer, 2003). Bevacizumab plus chemotherapy may work better than chemotherapy alone.

**How often do I receive the drug?** Bevacizumab is given by IV infusion, through a needle placed in a vein in the arm or hand, or through a central line (such as a port). The first time that bevacizumab is given, it will take about 90 minutes. After the first or second time—and once the doctor makes sure that you have no problems with the infusion—treatments with bevacizumab may require less time, usually about 30–60 minutes.

Bevacizumab is given in combination with chemotherapy. The recommended dose of bevacizumab is 5 mg/kg given once every 14 days for as long as the doctor recommends therapy.

**Possible serious side effects:** In clinical trials for colorectal cancer, a small percentage of people treated with bevacizumab in combination with chemotherapy experienced serious side effects, including gastrointestinal perforation (a hole in the wall of the intestine) and slow or incomplete wound healing. A very small percentage of people have died as a result of these serious side effects (Genentech, Inc., 2004).

Although bevacizumab is approved only for colorectal cancer, the drug also has been studied in different types of cancer. Some people receiving bevacizumab in combination with chemotherapy for lung cancer experienced tumor-related hemorrhage (bleeding at the site of the tumor). A small group of people receiving bevacizumab plus chemotherapy for breast cancer experienced congestive heart failure (failure of the heart to pump blood efficiently). Three people had taken a type of chemotherapy known as anthracyclines in the past or in combination with bevacizumab. Bevacizumab is not FDA approved for these or other types of cancer.

**Other side effects:** In clinical trials for colorectal cancer, hypertension (high blood pressure) and proteinuria (too much protein in the urine, which may be a sign of kidney damage) occurred more often in people receiving bevacizumab plus chemotherapy than in people receiving just chemotherapy. Standard oral medications were used to manage high blood pressure. Other side effects included weakness, pain, diarrhea, and leucopenia (a reduced white blood cell count) (Genentech BioOncology, 2004; Genentech, Inc., 2004).

Some people receiving bevacizumab in clinical trials experienced minor nosebleeding, which was generally mild and stopped on its own. If you experience a nosebleed, sit with your head tipped slightly forward and apply pressure by lightly pinching the bridge of your nose between the thumb and forefinger. Call your doctor if you feel dizzy or faint or if the bleeding does not stop in 10–15 minutes.

Because everyone is different, predicting what side effects you will experience is impossible. If you have questions about side effects or treatment with bevacizumab, talk to your doctor or another member of the healthcare team.

**What should I report to the physician or nurse?** The following should be reported immediately to your physician or nurse.

- Abdominal pain
- Light-headedness, dizziness, fainting, headache, broken blood vessels in your eyes, or a racing heart
- Bleeding that does not resolve on its own, such as nosebleeds, blood in the urine or stool, or a cut that will not stop bleeding
- Swelling in your feet or tenderness, pain, or warm areas in your thighs or legs
- Tightness or pain in your chest, difficulty breathing, coughing up blood, dizziness, light-headedness, or visual changes
- Fever higher than 101°F, severe chills, shaking, or itching

bevacizumab therapy. Patients who develop hypertension may require blood pressure monitoring at more frequent intervals. Patients with bevacizumab-induced or –exacerbated hypertension who discontinue bevacizumab should continue to have their blood pressure monitored at regular intervals.

- Monitor patients receiving bevacizumab for developing or worsening proteinuria with serial urinalysis per the clinic’s standard of care procedures. Patients with a urine dipstick reading of 2+ or higher should undergo further assessment with a 24-hour urine collection. Monitor patients with moderate to severe proteinuria regularly until improvement or resolution is observed.
  - Monitor patients closely for signs and symptoms of hemorrhage, such as epistaxis or any occult blood from the oral cavity or rectal or genitai-urinary area. Ask about the amount of bleeding that occurs from a wound or injury.
  - Assess for symptoms of thrombosis, such as pain in the abdomen, thighs, or legs; chest pain or pressure; shortness of breath; edema; skin discoloration or warmth, especially on extremities; dizziness; light-headedness; increased headaches; and visual disturbances. Educate patients about these signs and symptoms, and ensure that they understand their urgent nature and when to seek prompt medical care.
  - Pregnancy (category C): The risk to the fetus and nursing women is not known because of a lack of well-controlled studies. Angiogenesis is critical to fetal development, and the inhibition of angiogenesis following the administration of bevacizumab is likely to result in adverse effects on pregnancy. Whether bevacizumab is
excreted in human breast milk is unknown; therefore, bevacizumab should not be used in women not employing adequate contraception and only if the potential benefit justifies the potential risk to the fetus. Women should be advised to discontinue nursing during treatment with bevacizumab.

- The safety and effectiveness of bevacizumab in pediatric patients have not been studied. Analyses of demographic data suggest that no dose adjustments are necessary for age or sex.

**Patient education:** Patients should receive education about bevacizumab’s mechanism of action, treatment regimen, potential infusion reactions and side effects of chemotherapy, and when to call for medical assistance.

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**References**


