These Clinical Guidelines have been created using resources that were current as of the "Reviewed" date noted at the beginning of the document. Clinicians should refer to the manufacturer's Prescribing Information (or equivalent) for the most up-to-date information. While CarepathRx has published these Clinical Guidelines after a close review of available literature and a clinical review process, given the evolving nature and complexity of modern pharmaceutical products, CarepathRx does not and cannot warrant or guarantee that these Clinical Guidelines reflect the objectively best or highest standard of care at any given time.

Nothing within these Clinical Guidelines is intended to supersede or interfere with any individual clinician's decision-making or professional judgment with respect to either (1) prescribing or dispensing the drug or product in question or (2) the overall treatment plan for an individual patient.

Bevacizumab (Avastin) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
Policy ID: CG051
Effective: 5/15/2026
Reviewed: N/A
Revised: N/A
Approved by, Title and Date Approved: David Benedict, President, 5/15/26

I. BACKGROUND

Bevacizumab (Avastin) is a vascular endothelial growth factor inhibitor indicated for the treatment of multiple cancers such as metastatic colorectal cancer, recurrent glioblastoma, and metastatic renal cell carcinoma. It is a humanized monoclonal antibody that exerts its mechanism of action by interacting with receptors on endothelial cells. These endothelial cells, undisturbed, would proliferate and promote angiogenesis and the formation of new blood vessels. Bevacizumab inhibits the proliferation of endothelial cells, therefore preventing the microvascular development of tumors. There are several biosimilars on the market: Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), Alymsys (bevacizumab-maly), Avzivi (bevacizumab-tnjn), Jobevne (bevacizumab-nwgd), and Vegzelma (bevacizumab-adcd). The following outlines the procedures for servicing patients in need of outpatient bevacizumab infusions.

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:

1. Prescriber preference
2. Allergy profile
3. Age
4. Other relevant social and/or medical history

C. Physician orders for bevacizumab must include:

1. Patient weight
2. Drug
3. Dose (total dose and weight-based dose)
4. Route of administration
5. Frequency of administration
6. Emergency medications per protocol
7. Orders for pre-medications
8. Line care protocol
9. Routine lab monitoring, if applicable

D. Baseline labs or tests prior to starting therapy – Complete blood count (with differential), complete metabolic panel (CMP), and urine tests to measure proteinuria.

E. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See Appendix A (Nursing CarepathRx policy on *Management of Allergic/Anaphylactic Reactions*).

III. PHARMACOLOGY OVERVIEW

Refer to manufacturer's full Prescribing Information for most up to date information

A. Indications and Dosing

Indication	Dosing Regimen
Metastatic Colorectal Cancer	5mg/kg IV every 2 weeks in combination with bolus-IFL 10mg/kg IV every 2 weeks in combination with FOLFOX4 5mg/kg IV every 2 weeks or 7.5 mg/kg IV every 3 weeks in combination with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin-based chemotherapy in patients who have progressed on a first-line bevacizumab product-containing regimen
First-Line Non-Squamous Non-Small Cell Lung Cancer	15mg/kg IV every 3 weeks with carboplatin and paclitaxel
Recurrent Glioblastoma	10mg/kg IV every 2 weeks
Metastatic Renal Cell Carcinoma	10mg/kg IV every 2 weeks with interferon alfa
Persistent, Recurrent, or Metastatic Cervical Cancer	15 mg/kg IV every 3 weeks in combination with paclitaxel and cisplatin or in combination with paclitaxel and topotecan

Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer	Stage III or IV Disease Following Initial Surgical Resection - 15 mg/kg IV every 3 weeks in combination with carboplatin and paclitaxel for up to 6 cycles, followed by bevacizumab 15 mg/kg every 3 weeks as a single agent for a total of up to 22 cycles or until disease progression, whichever occurs earlier. Recurrent Disease (platinum resistant) - 10mg/kg IV every 2 weeks with paclitaxel, pegylated liposomal doxorubicin, or topotecan weekly. In combination with topotecan only, the dose is 15 mg/kg IV every 3 weeks. Recurrent Disease (platinum sensitive) - 15 mg/kg IV every 3 weeks, in combination with carboplatin and paclitaxel for 6 to 8 cycles, followed by bevacizumab 15 mg/kg every 3 weeks as a single agent until disease progression or 15 mg/kg IV every 3 weeks, in combination with carboplatin and gemcitabine for 6 to 10 cycles, followed by bevacizumab 15 mg/kg every 3 weeks as a single agent until disease progression.
Hepatocellular Carcinoma	5 mg/kg IV after administration of 1,200 mg of atezolizumab IV on the same day, every 3 weeks until disease progression or unacceptable toxicity

***Dosing is based off actual body weight. Bevacizumab has not been studied in extremes of body weights**

B. Dose Adjustment:

1. Renal Impairment: No dosage adjustment necessary
2. Liver Impairment: No dosage adjustment necessary
3. Bevacizumab can increase the risk of wound healing complications through the inhibition of vascular endothelial growth factor. Withhold bevacizumab for at least 28 days prior to elective surgery. Do not administer bevacizumab for at least 28 days following major surgery and until adequate wound healing.

C. Duration of therapy is dependent on patient response, adverse reactions, indication, and cycle regimen.

D. Contraindications: None

E. Warnings and Precautions:

1. Gastrointestinal Perforations and Fistula: Fatal cases have been reported. Discontinue for gastrointestinal perforations, tracheoesophageal fistula, grade 4 fistula, or fistula formation involving any organ. Incidence in clinical trials ranged from 0.3%-3%.
2. Surgery and Wound Healing Complications

    a. In patients who experience wound healing complications during bevacizumab treatment, withhold bevacizumab until adequate wound healing. Withhold for at least 28 days prior

to elective surgery. Do not administer bevacizumab for at least 28 days following major surgery, and until adequate wound healing. The safety of resumption of bevacizumab after resolution of wound healing complication has not been established. Discontinue for wound healing complication of necrotizing fasciitis.

3. Hemorrhage: Severe or fatal hemorrhages have occurred. Do not administer for recent hemoptysis. Discontinue for Grade 3-4 hemorrhage. Across clinical studies, 0.4%-7% of patients experienced grades 3-5 hemorrhagic events.
4. Arterial Thromboembolic Events (ATE) - risk of cerebral infarction, transient ischemic attacks (TIA), myocardial infarction (MI), and angina increased while using bevacizumab. Incidence of grades 3-5 events in clinical studies was 5%.
5. Venous Thromboembolic Events (VTE) - risk of deep vein thrombosis (DTV) and pulmonary embolism (PE) increased in patients using bevacizumab. Incidence of grade 3-4 events during clinical studies was 5%-11%.
6. Hypertension: Monitor blood pressure and treat hypertension. Withhold if not medically controlled; resume once controlled. Discontinue for hypertensive crisis or hypertensive encephalopathy. Across clinical studies, hypertension (grades 3-4) was reported with an incidence of 5%-18%.
7. Posterior Reversible Encephalopathy Syndrome (PRES): a neurological complication. Symptoms include headaches, seizures, visual disturbances, nausea, and vomiting. If PRES is identified, discontinue bevacizumab. Incidence in clinical studies was <0.5%.
8. Renal Injury and Proteinuria: Monitor urine protein. Discontinue for nephrotic syndrome. Withhold until less than 2 grams of protein in urine. Rates of proteinuria in clinical trials was 0.7%-7% (for grades 3 and 4).
9. Infusion-Related Reactions: Decrease rate for infusion-related reactions. Discontinue for severe infusion-related reactions and administer medical therapy.
10. Embryo-Fetal Toxicity: May cause fetal harm. Advise females of potential risk to fetus and need for use of effective contraception. See pregnancy and lactation below for more information.
11. Ovarian Failure: Due to the anti-VEGFA activity of bevacizumab. Counsel patients that fertility may be temporarily or permanently compromised after treatment with bevacizumab.
12. Congestive Heart Failure (CHF): Discontinue Bevacizumab in patients who develop CHF. Incidence of ovarian failure in clinical studies was 34% in premenopausal patients. The incidence of Grade 3 (or worse) left ventricular dysfunction was 1% in patients receiving bevacizumab. Risk may be increased in patients previously treated with anthracycline.
13. Pregnancy and lactation:

    a. Pregnancy: Bevacizumab may cause fetal harm per animal studies and limited post-marketing reports. Patients of child-bearing potential should be counseled on the risk bevacizumab has to fetal health and proper contraception should be encouraged during treatment (as well as for 6 months after the last dose).
    b. Lactation: No data is available regarding the presence of bevacizumab in human milk, the effects on the breast fed infant, or the effects on milk production. It is not recommended to breastfeed while being treated with bevacizumab, or for 6 months after the end of treatment. This is due to the role of VEGF in the development of the gastrointestinal tract during infancy.

14. Pediatrics:

    a. Safety and efficacy of bevacizumab have not been established in pediatric patients.

F. Pharmacokinetics:

1. Volume of Distribution: 2.9L
2. Half-life:
    a. Adult: ~20 days

G. Adverse Reactions:

1. >10%: Hypertension, peripheral edema, venous thromboembolism, exfoliative dermatitis, xeroderma, hyperglycemia, hypoalbuminemia, hypomagnesemia, hyponatremia, weight loss, abdominal pain, decreased appetite, diarrhea, dysgeusia, nausea, stomatitis, ovarian failure, pelvic pain, proteinuria, urinary tract infection, bruising, leukopenia, lymphocytopenia, neutropenia, thrombocytopenia, anxiety, dizziness, dysarthria, fatigue, headache, insomnia, myasthenia, voice disorders, arthralgias, back pain, limb pain, myalgias, increased serum creatinine, cough, dyspnea, epistaxis, oropharyngeal pain, pulmonary hemorrhage, sinusitis, postoperative wound complications.
2. 1-10%: arterial thrombosis, decreased left ventricular ejection fraction, deep vein thrombosis, heart failure, intra-abdominal venous thrombosis, left ventricular dysfunction, pulmonary embolism, syncope, thrombosis, acne vulgaris, cellulitis, dehydration, hypokalemia, constipation, gastritis, gastroesophageal reflux disease, gingivitis, hemorrhoids, oral mucosa ulcer, rectal fistula, hemorrhage, infusion-related reaction, infection, asthenia, deafness, tinnitus, nasal congestion, rhinorrhea.

H. Drug Interactions: Drug-drug interactions may exist. Consult interaction database for patient specific assessment.

1. It is not recommended that patients receiving immunotherapy receive live vaccines during therapy.

IV. ADMINISTRATIVE GUIDELINES

A. Administration:

1. The compounded sterile bevacizumab product is stable for 10 days in the refrigerator (2-8 degrees Celsius) at 1.4-16.5 mg/mL in polyvinyl chloride (PVC) bags per USP guidelines and current stability data.

B. Co-administration with other products in the same IV line: not compatible with dextrose-containing medications.

C. Hazardous handling: **This medication meets the definitions of a hazardous drug as outlined by the National Institute for Occupational Safety and Health (NIOSH). It is the responsibility of the dispensing pharmacy to ensure medication handling follows organizational policies and procedures.**

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol Swabs
2. Tape

3. Hazardous drug handling supplies:
    a. Chemotherapy gloves
    b. Protective gowns
    c. Chemotherapy prep mat
4. IV access supplies as applicable
    a. IV start Kit
    b. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
    c. Extension set 8" with needless connector
5. Port access supplies for patients with a port
    a. Port needle (ex. 22 Gauge x ¾ to 1" safe step)
    b. Needless connector
    c. Central line dressing change kit
6. Central IV access
    a. Needless connector
    b. Central line dressing change kit
7. IV Pole
8. IV administration set (flow regulator or gravity tubing)
9. Syringes (5 mL or 20 mL) with needles (20 G x 1")
10. Sharps container
11. Supplies if utilizing a pole mounted ambulatory infusion pump:
    a. Ambulatory pump tubing
    b. Pole mounted ambulatory pump
    c. Batteries for ambulatory pump (Ex: 9 Volt Duracell battery or 4 Double A batteries)
    d. Battery change procedure teaching sheet
    e. Continuous delivery mode teaching sheet
    f. Pump return box

B. Prescription items:

1. Compounded Avastin sterile product
2. Standard flushes per protocol
3. Anaphylaxis Kit

C. How Supplied:

1. 100 mg/4 mL (25 mg/mL)
2. 400 mg/16 mL (25 mg/mL)

D. Storage and Handling:

1. Store refrigerated at 2°C to 8°C (36°F to 46°F)
2. Protect from light

E. Compatibility:

1. Compatible with 0.9% saline
2. Not compatible with dextrose or dextrose-containing solutions

F. Procedures:

1. Explain the reasoning for visit and use of bevacizumab.

2. Don chemo gloves and gown. Prepare chemotherapy prep mat.
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication. Notify ordering physician and pharmacist if signs or symptoms are present.
4. Establish venous access if necessary.
5. Counsel patient on warnings, precautions, and potential side effects including but not limited to: hypertension, peripheral edema, ovarian failure (female patients), dizziness, anxiety, fatigue, arthralgia, dyspnea, infusion-related reactions, hemorrhage, and impairment of wound healing.
6. Administer the prepared compounded sterile product infusion based on the following infusion rates:
    a. Initial infusion: Infuse over 90 minutes
    b. Second infusion: Infuse over 60 minutes
    c. Subsequent infusions: If 60 minutes is tolerated, then administer all subsequent infusions over 30 minutes.
7. Post infusion monitoring: Monitor patient and vital signs periodically during the infusion and 30 minutes after the infusion is complete.

VI. CLINICAL MONITORING

A. Prior to therapy:

1. Baseline renal function, blood count, blood pressure, and echocardiography in high-risk patients

B. During therapy:

1. Blood pressure
2. Signs of peripheral edema
3. Infusion-related reactions
4. Impaired wound healing
5. Routine CBC and CMP

Please refer to the package insert for the most up to date guidance on this medication.

REFERENCES:

Avastin (Bevacizumab) [package insert]. Genetech; 2022.

United States Pharmacopeia (USP). General Chapter, <797> Pharmaceutical Compounding—Sterile Preparations. (2023) USP-NF. Rockville, MD: United States Pharmacopeia. Accessed November 29, 2023.

Gerriets V, Kasi A. Bevacizumab. [Updated 2023 Aug 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing

Seckute J, Castellanos I, Bane S. 3PC-038 Physicochemical stability of the bevacizumab biosimilar, ABP 215, in intravenous bags after preparation and storage. Section 3: Production and Compounding. Published online March 2020:A39.2-A39. doi:https://doi.org/10.1136/ejhpharm-2020-eahpconf.85

Einarsson J, Wilkinson AN. Vaccination considerations for patients receiving cancer therapy. Can Fam Physician. 2022;68(10):751-752. doi:10.46747/cfp.6810751

Bing Caryn, Nowobilski-Vasilios Anna et al. Extended Stability for Parenteral Drugs. Sixth Edition. American Society of Health Systems Pharmacists. Pages 176-7

APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS
Emergency Medication After Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

All other contents will not be needed.

Open the IM Epinephrine Bag

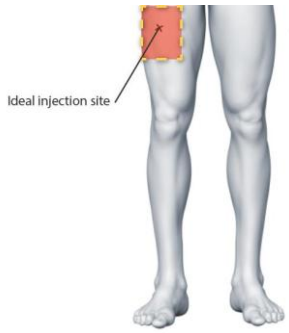
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an **alcohol swab, wipe the neck of the epinephrine ampule.**
3. Holding the ampule upright, **swirl and flick the ampule until all fluid flows to the bottom chamber** (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**

5. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampule and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
7. **Push the air out of the syringe by gently pushing on the plunger**.
8. Replace the cap on the brown filter needle. Discard remainder in ampule.
9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

Take the pills by mouth.

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.
Call 911 or have someone drive you to the emergency department.

APPENDIX B: EPINEPRINE KIT INSTRUCTIONS FOR IM INJECTION

Emergency Medication After Your Infusion

Please call 1-800-755-4704 if you have any questions or concerns. We are available 24 hours a day, 7 days a week. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.

Start with a clean work surface and clean hands.

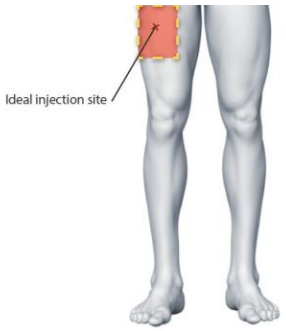
Open the supply bag labeled Epinephrine Kit Contents.

1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

2. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
3. Using an **alcohol swab, wipe the neck of the epinephrine ampule**
4. Holding the ampule upright, **swirl and flick the ampule until all fluid flows to the bottom chamber** (the top chamber should be empty).
5. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**
6. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **withdrawal all the medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
7. Remove the needle from the ampule and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
8. **Push the air out of the syringe by gently pushing on the plunger**.
9. Replace the cap on the brown filter needle.
10. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



2. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
1. **Push the needle into your leg muscle straight** in at a 90-degree angle.
2. **Inject the medication** by depressing the plunger in a slow and steady motion.
3. **Remove the needle** and wipe the site with the alcohol wipe.

Place all trash in the bag and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.

Call 911 or have someone drive you to the emergency department.