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.

Guidelines for Outpatient Gazyva (obinutuzumab) Therapy in Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis (Off Label)

Section: Clinical Guidelines
Compliance: ACHC Infusion Pharmacy
ACHC Standards:
URAC Standards:
Policy ID: NUR261
Effective: 6/1/2023
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Revised:
Approved by, Title and Date Approved: Kathleen Patrick, President, 6/1/2023

I. BACKGROUND

Gazyva (Obinutuzumab) is a glycoengineered monoclonal antibody that targets CD20, which activates the cell cycle in B-cells. It is currently approved for used in the treatment of chronic lymphocytic leukemia and follicular lymphoma, however recent case reports have shown promise in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis.

ANCA-associated vasculitis is a group of disorders characterized by inflammation and destruction of small- and medium-sized blood vessels and the presence of circulating ANCA. The cause and pathogenesis of ANCA-associated vasculitis are multifactorial and influenced by genetics, environmental factors, and responses of the immune system. Rituximab is a standard of care therapy for treatment of ANCA-associated vasculitis, however when all other conventional therapies have failed and rituximab is contraindicated, options are limited. Rituximab and Obinutuzumab are both anti-CD20 monoclonal antibodies, however Obinutuzumab has a slightly different mechanism making it efficacious for therapy in patients who have failed Rituximab or Rituximab is contraindicated due to hypersensitivity reactions.

Obinutuzumab binds to CD20 expressed on the surface of pre B- and mature B-lymphocytes. This activates complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity, and antibody-dependent cellular phagocytosis, resulting in cell death. Because it is a type II anti-CD20 monoclonal antibody, it has greater direct B-cell killing effects and lower complement-dependent cytotoxicity compared to other anti-CD20 monoclonal antibodies like Rituximab.

Currently only three case studies have been published to support Obinutuzumab use in this patient population. The following includes information obtained from these case reports and package insert/ manufacturer details and outlines the procedures for servicing patients in need of outpatient Obinutuzumab 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. All patients should receive first dose of obinutuzumab in a controlled setting due to the high incidence of infusion and anaphylaxis reactions. Date of prior infusion should be provided.
C. The decision to administer subsequent doses in the home by a home infusion 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 ≥18 years
4. Other relevant social and/or medical history

D. Physician orders for obinutuzumab must include:

1. Drug and dose
2. Route of administration
3. Frequency of administration
4. Emergency medications
5. Orders for pre-medications
6. Line care protocol
7. Routine lab monitoring, if applicable

E. Baseline labs or tests prior to starting therapy

1. CBC, platelets, and CMP
2. Hepatitis B virus (HBV) screening (hepatitis B surface antigen, hepatitis B core antibody, total Ig or IgG, and antibody to hepatitis B surface antigen prior to beginning of therapy)

F. Vaccination status – Ensure patients are up to date on vaccinations. If possible, the patient should be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating obinutuzumab.

G. For subsequent infusions in the home setting, dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See policy NUR012 (Appendix A).

III. PHARMACOLOGY OVERVIEW

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

A. Indications - **Only autoimmune/inflammation related indications are covered for the purpose of this guideline*

1) ANCA-associated vasculitis (off-label)
   a) After more conventional therapies failed and Rituximab is contraindicated

B. Dosage

1. Table 1: Dose schedule for ANCA-associated vasculitis specific to case report series

Day of treatment cycle		Dose of Gazyva
Cycle 1 (Induction)	Day 1	1000 mg
	Day 15	1000 mg
Cycle 2+ (Maintenance)	Every 6 months	1000 mg

C. Contraindications

1. Known hypersensitivity reactions (e.g., anaphylaxis) to obinutuzumab or to any of the excipients, or serum sickness with prior obinutuzumab

D. Warnings and Precautions

1. Hepatitis B Virus Reactivation
   a. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur. HBV reactivation has been reported in patients who are hepatitis B surface antigen (HBsAg) positive and also in patients who are HBsAg negative but are hepatitis B core antibody (anti-HBc) positive. Reactivation has also occurred in patients who appear to have resolved hepatitis B infection (i.e.,

HBsAg negative, anti-HBc positive, and hepatitis B surface antibody [anti-HBs] positive).

b. Screen all patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with obinutuzumab. For patients who show evidence of hepatitis B infection (HBsAg positive [regardless of antibody status] or HBsAg negative but anti-HBc positive), consult healthcare providers with expertise in managing hepatitis B regarding monitoring and consideration for HBV antiviral therapy.

c. In patients who develop reactivation of HBV while receiving obinutuzumab, immediately discontinue obinutuzumab and any concomitant chemotherapy and institute appropriate treatment. Resumption of obinutuzumab in patients whose HBV reactivation resolves should be discussed with healthcare providers with expertise in managing hepatitis B. Insufficient data exist regarding the safety of resuming obinutuzumab in patients who develop HBV reactivation.

2. Progressive Multifocal Leukoencephalopathy
    a. John Cunningham (JC) virus infection resulting in progressive multifocal leukoencephalopathy (PML), which can be fatal, has occurred. Consider the diagnosis of PML in any patient presenting with new onset or changes to preexisting neurologic manifestations. Evaluation of PML includes, but is not limited to, consultation with a neurologist, brain MRI, and lumbar puncture. Discontinue obinutuzumab therapy and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML.
3. Infusion-Related Reactions (IRRs)
    a. Obinutuzumab can cause severe and life-threatening infusion-related reactions (IRRs). Sixty-five percent of patients with CLL experienced a reaction to the first 1,000 mg dose of obinutuzumab infused. Thirty-seven percent of patients with relapsed or refractory NHL and 60% of patients with previously untreated NHL experienced a reaction on Day 1 of obinutuzumab infusion. IRRs have occurred within 24 hours of receiving obinutuzumab. IRRs can also occur with subsequent infusions. Symptoms may include hypotension, tachycardia, dyspnea, and respiratory symptoms (e.g., bronchospasm, larynx and throat irritation, wheezing, laryngeal edema). The most frequently reported symptoms include nausea, fatigue, chest discomfort, dyspnea, dizziness, vomiting, diarrhea, rash, hypertension, hypotension, flushing, headache, pyrexia, and chills.
    b. Premedicate patients with acetaminophen, antihistamine, and a glucocorticoid. Closely monitor patients during the entire infusion. Reduce infusion rate, interrupt infusion or permanently discontinue obinutuzumab for IRRs based on severity.
    c. For patients with preexisting cardiac or pulmonary conditions, monitor more frequently throughout the infusion and the post-infusion period since they may be at greater risk of experiencing more severe reactions. Hypotension may occur as part of the IRR to obinutuzumab. Consider risk vs benefit in withholding antihypertensive treatments for 12 hours prior to, during each obinutuzumab infusion, and for the first hour after administration until blood pressure is stable.
4. Hypersensitivity Reactions Including Serum Sickness
    a. Hypersensitivity reactions have been reported. Signs of immediate-onset hypersensitivity included dyspnea, bronchospasm, hypotension, urticaria and tachycardia. Late-onset hypersensitivity diagnosed as serum sickness has also been reported, with symptoms that include chest pain, diffuse arthralgia and fever. Hypersensitivity reactions may be difficult to clinically distinguish from IRRs. However, hypersensitivity very rarely occurs with the first infusion and, when observed, often occurs after previous exposure.

b. If a hypersensitivity reaction is suspected during or after an infusion, stop the infusion and permanently discontinue treatment. Obinutuzumab is contraindicated in patients with known hypersensitivity reactions to obinutuzumab, including serum sickness with prior obinutuzumab use.

5. Tumor Lysis Syndrome
    a. Tumor lysis syndrome (TLS), including fatal cases, has been reported. Patients with high tumor burden, high circulating lymphocyte count (> 25 x 10^9/L) or renal impairment are at greater risk for TLS.
    b. Administer appropriate tumor lysis prophylaxis with anti-hyperuricemics (e.g., allopurinol or rasburicase) and hydration prior to the infusion of obinutuzumab for patients at risk for TLS. During the initial days of obinutuzumab treatment, monitor the laboratory parameters of patients considered at risk for TLS. For treatment of TLS, correct electrolyte abnormalities, monitor renal function and fluid balance, and administer supportive care, including dialysis as indicated.
    c. TLS requires urgent medical treatment and hospitalization.
6. Infections
    a. Fatal and serious bacterial, fungal, and new or reactivated viral infections can occur during and following obinutuzumab therapy. Grade 3 to 5 infections have been reported in up to 8% of patients during combination therapy, up to 13% of patients during monotherapy, and up to 8% of patients after treatment.
    b. Do not administer obinutuzumab to patients with an active infection. Patients with a history of recurring or chronic infections may be at increased risk of infection.
7. Neutropenia
    a. Severe and life-threatening neutropenia, including febrile neutropenia, has been reported. Monitor patients with Grade 3 to 4 neutropenia frequently with regular laboratory tests until resolution. Anticipate, evaluate, and treat any symptoms or signs of developing infection. Consider dose delays for Grade 3 or 4 neutropenia. Consider administration of granulocyte colony-stimulating factors (GCSF) in patients with Grade 3 or 4 neutropenia.
    b. Neutropenia can also be of late onset (occurring more than 28 days after completion of treatment) and/or prolonged (lasting longer than 28 days). Patients with severe and long lasting (> 1 week) neutropenia are strongly recommended to receive antimicrobial prophylaxis until resolution of neutropenia to Grade 1 or 2. Consider antiviral and antifungal prophylaxis.
8. Thrombocytopenia
    a. Severe and life-threatening thrombocytopenia has been reported. Fatal hemorrhagic events have been reported in patients treated with obinutuzumab in combination with chemotherapy, including during Cycle 1.
    b. Monitor all patients frequently for thrombocytopenia and hemorrhagic events, especially during the first cycle and if clinically indicated, evaluate laboratory coagulation parameters. In patients with Grade 3 or 4 thrombocytopenia, monitor platelet counts more frequently until resolution and consider dose delays of obinutuzumab and chemotherapy or dose reductions of chemotherapy. Transfusion of blood products (i.e., platelet transfusion) may be necessary. Consider withholding concomitant medications that may increase bleeding risk (platelet inhibitors, anticoagulants), especially during the first cycle.
9. Disseminated Intravascular Coagulation (DIC)
    a. Fatal and severe DIC has been reported. The majority of DIC cases have involved changes in platelets and laboratory coagulation parameters following the first infusion, with spontaneous resolution usually occurring by Day 8. In some cases, DIC was associated with IRRs, TLS, or both. In patients with suspected DIC,

evaluate potential causes, and monitor coagulation parameters, platelet counts, and for signs and symptoms of bleeding or thrombosis. Manage according to standard guidelines for DIC. Supportive care, including transfusion of blood products and other medical management, may be necessary.

10. Immunization
    a. The safety and efficacy of immunization with live or attenuated viral vaccines during or following obinutuzumab therapy have not been studied. Immunization with live virus vaccines is not recommended during treatment and until B-cell recovery.
11. Embryo-Fetal Toxicity
    a. Based on its mechanism of action and findings in animals, obinutuzumab can cause B-cell depletion in infants exposed to obinutuzumab in-utero. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception while receiving obinutuzumab and for 6 months after the last dose.

E. Pharmacokinetics
    A. Vd: ~4.1 to 4.3 L.
    B. Half-life: 25.5 to 35.3

F. Adverse Reactions (
1. > 10%
    a. **Dermatologic**: Pruritus (11%), skin rash (monotherapy: ≥10%; combination therapy: 17%)
    b. **Endocrine & metabolic**: Hyperkalemia (20% to 33%), hypernatremia (16%), hyperuricemia (28%), hypoalbuminemia (23% to 33%), hypocalcemia (32% to 39%), hypokalemia (14%), hyponatremia (26%), hypophosphatemia (36% to 41%)
    c. **Gastrointestinal**: Constipation (8% to 32%) decreased appetite (14%), diarrhea (monotherapy: ≥10%; combination therapy: 10% to 30%; grades 3/4: 2% to 3%)
    d. **Genitourinary**: Urinary tract infection (monotherapy: ≥10%; combination therapy: 5% to 13%)
    e. **Hematologic & oncologic**: Anemia (12% to 39%; grades 3/4: 5% to 10%), hemorrhage (12%; grades 3/4: 4%), hypoproteinemia (32%), leukopenia (84% to 92%; grades 3/4: 17% to 49%), lymphocytopenia (monotherapy: grades 3/4: 5% to 23%; combination therapy: 80% to 97%; grades 3/4: 33% to 92%), neutropenia (monotherapy: 13% to 20%; grades 3/4: 10% to 25%; combination therapy: 37% to 84%; grades 3/4: 33% to 59%; onset ≥28 days after completion of treatment: 4% to 16%; lasting ≥28 days: 1% to 3%), thrombocytopenia (14% to 68%; grades 3/4: 7% to 13%; onset within 24 hours of infusion: 4%)
    f. **Hepatic**: Hyperbilirubinemia (21%), increased serum alanine aminotransferase (28% to 50%), increased serum alkaline phosphatase (18% to 27%), increased serum aspartate aminotransferase (27% to 44%)
    g. **Hypersensitivity:** Infusion-related reaction (monotherapy: 8% to 9%; combination therapy: 66% to 72%, cycle 1: 37% to 65%, subsequent cycles: ≤23% [dependent on dose, cycle, and use of premedications]; can be severe infusion-related reaction)
    h. **Infection**: Herpes virus infection (monotherapy: 13%; combination therapy: 18%), infection (38% to 82%)
    i. **Nervous system**: Fatigue (monotherapy: ≥10%; combination therapy: 40%), headache (18%), insomnia (15%)
    j. **Neuromuscular & skeletal**: Arthralgia (12% to 16%), musculoskeletal signs and symptoms (including musculoskeletal pain: monotherapy: 20%; combination therapy: 18% to 54%)
    k. **Renal**: Increased serum creatinine (30%)

l. **Respiratory**: Cough (monotherapy: 23%; combination therapy: 10% to 35%), pneumonia (14%), respiratory tract infection (monotherapy: ≥10%; combination therapy: 14%), upper respiratory tract infection (monotherapy: 40%; combination therapy: 36% to 50%)
m. **Miscellaneous**: Fever (9% to 19%)

2. < 10%
   a. **Hematologic & oncologic**: Febrile neutropenia (6%), tumor lysis syndrome (grades 3/4: ≤2%), Disseminated intravascular coagulation (<1%)
   b. **Immunologic**: Antibody development (≤7%)
   c. **Infection**: Sepsis (7%)
   d. **Neuromuscular & skeletal**: Back pain (5%)
   e. **Respiratory**: Nasopharyngitis (6%)

G. Drug Interactions
1. Concurrent use with other immunosuppressants and myelosuppressive agents enhance their respective effects.
2. Concurrent use of live vaccines may enhance the risk of vaccine-associated infection.
3. Concurrent use with agents with antiplatelet properties and anticoagulants may increase the risk of serious bleeding-related events associated with obinutuzumab.
4. Concurrent use of other blood pressure-lowering agents may enhance hypotensive effects.

IV. ADMINISTRATIVE GUIDELINES

A. Administration
1. Patients should receive their first infusion in a controlled setting. All patients will require an anaphylaxis kit in the home for subsequent infusions due to the risk of serious infusion reactions.
2. IV infusions should be given immediately after reconstitution and dilution. Use within 1 hour of preparation per current USP Immediate-Use Guidelines. **No filter tubing is needed.**
3. Do not mix or dilute with other drugs. Do not administer as an intravenous push or bolus.
4. Dilute into a 0.9% Sodium Chloride Injection, USP PVC or non-PVC polyolefin infusion bag.
5. Pre-medicate prior to each obinutuzumab infusion to reduce infusion-related reactions
   A. Considerations for premedications were not explicitly discussed in case reports however considering the hypersensitivity risk of this medication, would consider premedication for patients. Recommendations are included in the chart below and are based on provider discretion.

Day of Treatment Cycle	Patients requiring premedication	Premedication	Administration
Induction Day 1	All patients	Intravenous glucocorticoid: 20 mg dexamethasone or 80 mg Methylprednisolone [1,2]	Completed at least 1 hour prior to GAZYVA infusion.
		650–1,000 mg acetaminophen	At least 30 minutes before GAZYVA infusion.
		anti-histamine (e.g., 50 mg diphenhydramine)	
Induction Day 15 and	All patients	650–1,000 mg acetaminophen	At least 30 minutes before

Subsequent Maintenance Cycles			GAZYVA infusion.
	Patients with an IRR (Grade 1-2) with the previous infusion	650–1,000 mg acetaminophen	At least 30 minutes before GAZYVA infusion.
		anti-histamine (e.g., 50 mg diphenhydramine)	
	Patients with a Grade 3 IRR with the previous infusion OR with a lymphocyte count > 25 x 109 /L prior to next treatment	Intravenous glucocorticoid: 20 mg dexamethasone or 80 mg methylprednisolone [1]	Completed at least 1 hour prior to GAZYVA infusion.
		650–1,000 mg acetaminophen	At least 30 minutes before GAZYVA infusion.
		anti-histamine (e.g., 50 mg diphenhydramine)	

B. Duration
   1. Duration of therapy should be dependent on patient response, disease progression, and adverse reactions.

C. Dose adjustments
   1. Missed doses
      A. If a planned dose of obinutuzumab is missed, administer the missed dose as soon as possible.
   2. Adverse reactions adjustments
      A. Reduce infusion rate, interrupt infusion or permanently discontinue obinutuzumab for IRRs based on severity. Institute medical management (e.g., glucocorticoids, epinephrine, bronchodilators, and/or oxygen) for IRRs as needed.
         (1) **Grade 4 (life-threatening)**: Stop infusion immediately and permanently discontinue obinutuzumab.
         (2) **Grade 3 (severe)**: Interrupt infusion and manage symptoms.
         (a) For patients who experience Grade 3 IRRs during standard infusion, upon resolution of symptoms, consider restarting obinutuzumab infusion at no more than half the previous rate (the rate being used at the time that the IRR reaction occurred), and if patient does not experience any further IRR symptoms, infusion rate escalation may resume at the increments and intervals as appropriate for the treatment cycle dose. Permanently discontinue treatment if patients experience a Grade 3 or higher IRR at rechallenge.
         (3) **Grade 1–2 (mild to moderate)**: Reduce infusion rate or interrupt infusion and manage symptoms. Upon resolution of symptoms, continue or resume obinutuzumab infusion, and if patient does not experience any further IRR symptoms, infusion rate escalation may resume at the increments and intervals as appropriate for the treatment cycle dose.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:
   1. Alcohol Swabs
   2. Gloves

3. Dressing change kit
4. IV Pole and pole clamp
5. IV Start Kit for peripheral line
6. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾" for patients needing peripheral access)
7. Port access needle (ex. 22 Gauge x ¾ to 1" safe step)
8. Extension set 8"
9. IV injection cap
10. Administration tubing ((PVC) or non-PVC polyolefin sets)
11. Pole mounted infusion pump
12. Syringe with needle
13. Batteries for pump administration
14. Sharps container
15. Tape

B. Prescription items:
1. Obinutuzumab vials
2. 250 mL of NS

C. How Supplied
1. Clear, colorless to slightly brown, preservative-free solution for intravenous use supplied as 1,000 mg/40 mL (25 mg/mL) in single-dose vials

D. Storage and Handling
1. Store vials refrigerated between 2 and 8 degrees C (36 and 46 degrees F). Protect from light. Do not shake or freeze.

E. Compatibility
1. Compatible in NS only

F. Procedures: Preparation of product, Infusion rates, post infusion monitoring time.
A. Explain the reasoning for visit and use of obinutuzumab.
B. Don gloves.
C. Establish venous access prior to preparation of drug.
D. After establishing access, it is recommended to pre-medicate with acetaminophen and antihistamines 30 minutes prior to infusion, glucocorticoids 60 minutes prior to infusion. Premedication recommendations may differ based on the Grade of IRR from the previous infusion(s).
E. Counsel patient on warnings, precautions, and potential side effects including but not limited to: HBV reactivation, PML, IRRs, hypersensitivity reactions including serum sickness, TLS, infections, neutropenia, thrombocytopenia, DIC, and embryo-fetal toxicity.
F. Use appropriate aseptic technique. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not use vial if particulates or discoloration is present.
G. Cycle 1, Day 1, 1000 mg dose (Induction) should be administered in a controlled setting and will not be discussed in this clinical guideline
H. Cycle 1 Day 15, 1000 mg dose (Induction) and subsequent maintenance doses
(1) Withdraw 40 mL of obinutuzumab from the vial and inject into 250 mL 0.9% sodium chloride bag.
I. Gently invert the bag to mix the solution. Discard any unused portion left in the vial. Attach pump tubing to compounded product bag and prime tubing. Infuse via electric pump. The product can be administered at a final concentration of 0.4 mg/mL to 4 mg/mL.
J. Infusion Rates

Day of treatment cycle		Dose of Gazyva	Rate of Infusion
Cycle 1 (Induction)	Day 1	1000 mg	*Should be administered in a controlled setting and will not be discussed in this clinical guideline
	Day 15	1000 mg	**If no reaction or grade 1 reaction to previous infusion and the final infusion rate was 100 mg/hour or faster**, initiate infusion at 100 mg/hour for 30 minutes; if tolerated, may escalate rate in increments of 100 mg/hour every 30 minutes to a maximum rate of 400 mg/hour. **If a grade 2 or higher infusion reaction occurred during the previous infusion**, initiate infusion at 50 mg/hour for 30 minutes; if tolerated, may escalate rate in increments of 50 mg/hour every 30 minutes to a maximum rate of 400 mg/hour.
Cycle 2+ (Maintenance)	Every 6 months	1000 mg	

K. Monitor patient and vital signs periodically during the infusion and for 30 minutes after the completion of the infusion per INS guidelines.

VI. CLINICAL MONITORING

A. Prior to therapy:
   (a) HBV screening
   (b) CBC with platelets
   (c) CMP
   (d) Pregnancy status
   (e) Ensure patient is up to date on vaccines per CDC guidelines.

B. During therapy:
   1. Assessment of signs/symptoms of adverse effects:
      A. Hypersensitivity reactions
      B. Hepatitis B virus reactivation
      C. Tumor lysis syndrome
      D. Active infection
      E. Blood dyscrasias – thrombocytopenia, neutropenia, signs/symptoms of bleeding
      F. Progressive Multifocal Leukoencephalopathy (PML) - focal neurologic deficits, which may present as hemiparesis, visual field deficits, cognitive impairment, aphasia, ataxia, and/or cranial nerve deficits
      G. Hypotension (if on other medications that lower blood pressure)
      H. Common adverse reactions (incidence ≥ 20%) Neutropenia, IRRs, fatigue, cough, upper respiratory tract infections, musculoskeletal pain, constipation, diarrhea
   2. Obinutuzumab can cause fetal harm. Advise females of reproductive age of potential risks and to use effective contraception while receiving obinutuzumab and for 6 months after the last dose.
   3. Labs:
      A. CBC with differential regularly; If DIC suspected: coagulation parameters and platelet counts
      B. CMP periodically throughout therapy

C. LFT's –during and for up to 12 months after therapy completion

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

REFERENCES:

GAZYVA (obinutuzumab) [prescribing information]. South San Francisco, CA: Genentech, Inc; 2022.

Amudala, N. A., Boukhlal, S., Sheridan, B., Langford, C. A., Geara, A., Merkel, P. A., & Cornec, D. (2022). Obinutuzumab as treatment for ANCA-associated vasculitis. Rheumatology (Oxford, England), 61(9), 3814–3817. https://doi.org/10.1093/rheumatology/keab916

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

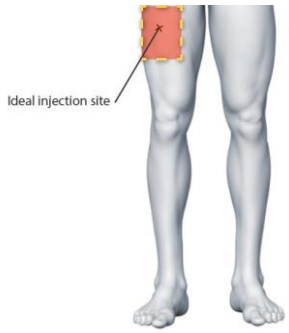
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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.