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Obinutuzumab (Gazyva) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline

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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 use in the treatment of chronic lymphocytic leukemia, follicular lymphoma, and lupus nephritis. Obinutuzumab has also shown promise in a small case series and cohort study in patients with antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis who were rituximab-intolerant.

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. Options are limited when conventional therapies have failed and rituximab is contraindicated. 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.

The following 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. 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. Patient has a diagnosis of lupus nephritis or other autoimmune disease state. ***Only patients with lupus nephritis or autoimmune diagnoses are eligible for home treatment***
 - 5. Other relevant social and/or medical history

6. Recent baseline CBC with differential

C. Physician orders for obinutuzumab must include:

1. Drug and dose
2. Route of administration
3. Frequency of administration
4. Emergency medications per protocol
5. Orders for pre-medications
6. Order for concurrent 250 mL 0.9% sodium chloride IV hydration if approved for first dose at home
7. Line care protocol
8. Routine lab monitoring, if applicable

D. Baseline labs or tests prior to starting therapy

1. Recent CBC with differential
2. Complete metabolic panel (CMP)
3. Hepatitis B virus (HBV) screening
4. 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.

E. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician.

See Appendix A (CarepathRx Nursing 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 - **Only autoimmune/inflammatory-related indications are covered for the purpose of this guideline**

1. Treatment of lupus nephritis in adult patients receiving standard therapy
2. Treatment of ANCA-associated vasculitis (off-label) after failure of conventional therapies and rituximab is contraindicated

B. Dosing:

1. **Lupus nephritis:** 1000 mg IV on day 1, followed by 1000 mg IV on weeks 2, 24, and 26 (14 days after dose 3); followed by 1000 mg IV every 6 months from doses 5 and beyond (dose 5 should be administered 6 months after dose 4)
2. **ANCA-associated vasculitis** specific to case report series:
 - a. Cycle 1 (Induction): 1000 mg IV on Day 1 and 1000 mg IV on Day 15
 - b. Cycle 2+ (Maintenance): 1000 mg IV every 6 months

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

C. Dose Adjustment

1. Delayed or missed doses: if a planned infusion is missed, administer as soon as possible. Do not wait until the next scheduled infusion. The administration schedule should be adjusted to maintain the appropriate interval between doses.
 2. No dose adjustments for renal or hepatic impairment.
 3. Adverse reactions adjustments: Reduce infusion rate, interrupt infusion or permanently discontinue obinutuzumab for infusion related reactions based on severity. Institute medical management (e.g., glucocorticoids, epinephrine, bronchodilators, and/or oxygen) for IRRs as needed.
 - a. **Grade 4 (life-threatening):** Stop infusion immediately and permanently discontinue obinutuzumab.
 - b. **Grade 3 (severe):** Interrupt infusion and manage symptoms. 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.
 - c. **Grade 1–2 (mild to moderate):** Reduce infusion rate to half the rate that was used at the time of reaction and treat symptoms. Once symptoms are resolved, keep the infusion at the same reduced rate for an additional 30 minutes. If there are no further symptoms of IRR, infusion rate can be increased at the increments appropriate for the treatment dose.
- D. Duration of therapy: dependent on patient response and adverse reactions
- E. Contraindications: Known hypersensitivity reactions (e.g., anaphylaxis) to obinutuzumab or to any of the excipients, or serum sickness with prior obinutuzumab.
- F. Warnings and Precautions
1. **Hepatitis B Virus Reactivation:** 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 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).
 2. 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.
 3. 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.
 4. **Progressive Multifocal Leukoencephalopathy:** 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.

5. **Infusion-Related Reactions (IRRs):** 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. IRRs in patients with lupus nephritis mainly occurred during the first infusion. These reactions were mostly mild to moderate and managed by slowing the infusion rate. Severe and life-threatening reactions were reported and needed symptomatic treatment. The most common IRRs in the lupus nephritis studies were headache, nausea, vomiting, pyrexia, and tachycardia.

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.

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 versus 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.

- a. **Hypersensitivity Reactions Including Serum Sickness:** 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 is very rarely an occurrence with the first infusion and, when observed, often occurs after previous exposure. 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.
- b. **Tumor Lysis Syndrome:** Tumor lysis syndrome (TLS), including fatal cases, has been reported. Patients with high tumor burden, high circulating lymphocyte count ($> 25 \times 10^9/L$) or renal impairment are at greater risk for TLS.

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. TLS requires urgent medical treatment and hospitalization.

- c. **Serious, Including Fatal Infections:** 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 11% of patients with lupus nephritis who received obinutuzumab and standard treatment compared to 9% patients who received placebo and standard therapy in clinical studies within 52 weeks to 76 weeks. These incidences corresponded to an exposure-adjusted incidence rate of 8.9 (obinutuzumab) and 7.9 (placebo) per 100 patient years. Fatal reactions occurred in 1% (2/200 patients) treated with obinutuzumab and 0.5% (1/193 patients) of the placebo and standard therapy group. 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.

- d. **Neutropenia:** 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. 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.
- e. **Thrombocytopenia:** 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. 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.
- f. **Disseminated Intravascular Coagulation (DIC):** 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.
- g. **Immunization:** 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.
- h. **Embryo-Fetal Toxicity:** 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.
- i. **Pregnancy and Lactation:** Fetal risk may occur when used during pregnancy. See *Embryo-Fetal Toxicity* under *Warnings and Precautions* for more information. Obinutuzumab crosses the placenta. Pregnant women with systemic lupus erythematosus have a greater risk of adverse pregnancy outcomes, such as premature birth, miscarriage, intrauterine growth restriction, and worsening of underlying disease. Lupus nephritis increases the risk of hypertension,

preeclampsia, and eclampsia in expectant mothers. Autoantibodies that cross the placenta may result in adverse neonatal outcomes, including neonatal lupus and congenital heart block. Live vaccines should be avoided to neonates exposed in utero until B-cell recovery occurs. The risk of fetal harm cannot be ruled out in breastfeeding mothers receiving obinutuzumab therapy and the benefits of treatment must be weighed against the potential risk to the breastfeeding infant.

G. Pharmacokinetics

1. Vd: ~4.1 to 4.3 L.
2. Half-life: 22.4 to 35.3 days

H. Adverse Reactions:

1. Serious:
 - a. **Gastrointestinal:** Gastrointestinal perforation
 - b. **Hematologic:** Anemia, grade 3 or 4 (5%), Disseminated intravascular coagulation (0.3%), Febrile neutropenia, Hemorrhage, Leukopenia, grade 3 or 4 (4% to 5%), Neutropenia, all grades (14% to 53%), Neutropenia, grade 3 or higher (7% to 49%), Thrombocytopenia, all grades (14%), Thrombocytopenia, grade 3 or higher (10%)
 - c. **Hepatic:** Reactivation of hepatitis B viral hepatitis
 - d. **Immunologic:** Hypersensitivity reaction
 - e. **Neurologic:** Progressive multifocal leukoencephalopathy
 - f. **Renal:** Urinary tract infectious disease (5% to 21%)
 - g. **Respiratory:** COVID-19 (23%), Pneumonia (10% to 14%)
 - h. **Miscellaneous:** Infectious disease (38% to 82%), Infusion reaction (10% to 72%), Tumor lysis syndrome, grade 3 or 4 (2%)
2. Common:
 - a. **Dermatologic:** Alopecia
 - b. **Gastrointestinal:** Constipation (8%), Diarrhea (10%)
 - c. **Hematologic:** Anemia, all grades (12%)
 - d. **Immunologic:** Herpes simplex virus infection
 - e. **Musculoskeletal:** Arthralgia (12% to 16%), Musculoskeletal pain (28%)
 - f. **Neurologic:** Headache, Insomnia
 - g. **Respiratory:** Bronchitis (14%), Cough (10% to 35%), Upper respiratory infection (29% to 50%)
 - h. **Miscellaneous:** Fatigue (40%), Fever (9% to 19%)

I. 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.
5. Drug-drug interactions may exist. Consult interaction database for patient specific assessment.

IV. ADMINISTRATIVE GUIDELINES

- A. Administration: IV infusions should be given immediately after reconstitution and dilution. Use within 4 hours of preparation per current USP Immediate-Use Guidelines.
- B. Do not mix or dilute with other drugs. Do not administer as an intravenous push or bolus.
- C. Pre-medicate prior to each obinutuzumab infusion to reduce infusion-related reactions:

Lupus Nephritis Pre-medications for All Patients For Each Infusion*	
Intravenous glucocorticoid (methylprednisolone 80 mg IV)*	Completed 30-60 minutes before obinutuzumab infusion *Starting from dose 6, IV corticosteroid should only be infused in patients who have experienced an IRR in the prior infusion
Acetaminophen 650-1000 mg	
Antihistamine (e.g. 50 mg diphenhydramine)	

ANCA-Associated Vasculitis Pre-medications*			
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 infusion.
		650–1,000 mg acetaminophen	At least 30 minutes before infusion.
		antihistamine (e.g., 50 mg diphenhydramine)	
Induction Day 15 and Subsequent Maintenance Cycles	All patients	650–1,000 mg acetaminophen	At least 30 minutes before infusion.
	Patients with an IRR (Grade 1-2) with the previous infusion	650–1,000 mg acetaminophen	At least 30 minutes before infusion.
		antihistamine (e.g., 50 mg diphenhydramine)	
	Patients with a Grade 3 IRR with the previous infusion OR	Intravenous glucocorticoid: 20 mg dexamethasone or 80 mg methylprednisolone ¹	Completed at least 1 hour prior to infusion.
		650–1,000 mg	At least 30

	with a lymphocyte count > 25 x 10 ⁹ /L prior to next treatment	acetaminophen	minutes before infusion.
		antihistamine (e.g., 50 mg diphenhydramine)	

*ANCA- associated vasculitis: considerations for pre-medications were not explicitly discussed in case reports or cohort study but considering the hypersensitivity risk of this medication, would consider premedication for patients. Recommendations are included in the chart above and are based on provider discretion.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol Swabs
2. Gloves
3. Tape
4. IV access supplies as applicable
 - a. Peripheral IV access supplies for patients requiring peripheral IV access
 - 1) IV start kit
 - 2) Peripheral IV catheter (ex. 22 Gauge x 1" and 24 Gauge x ¾")
 - 3) Extension set 8" with needless connector
 - b. Port access supplies for patients with a port
 - 1) Port needle (ex. 22 Gauge x ¾ to 1" safe step)
 - 2) Needless connector
 - 3) Central line dressing change kit
5. IV Pole
6. Syringes (20-60 mL) with needles (20 Gauge x 1")
7. Sharps container
8. Pole-mounted infusion pump
9. Ambulatory pump tubing
10. Batteries for ambulatory pump (Ex: 9 Volt Duracell battery or 4 Double A batteries)
11. Battery change procedure teaching sheet
12. Continuous delivery mode teaching sheet
13. Pump return box
14. For normal saline hydration with any first doses:
 - a. IV administration set (flow regulator or gravity tubing)
 - b. Y-site IV connector

B. Prescription items:

1. Obinutuzumab vial(s)
2. 250 mL of 0.9% sodium chloride (diluent bag)
3. Pre-medications: acetaminophen, antihistamine, glucocorticoid (*refer to Administration Guidelines listed above*)

4. Additional 250 mL 0.9% sodium chloride bag (for first dose at home)
 5. Standard flushes per protocol
 6. Anaphylaxis kit per protocol
- C. How Supplied: 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: Store vials refrigerated between 2 and 8 degrees C (36 and 46 degrees F). Protect from light. Do not shake or freeze.
- E. Compatibility: Compatible in 0.9% sodium chloride only
- F. Procedures:
1. Explain the reasoning for visit and use of obinutuzumab.
 2. Don gloves.
 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 prior to preparation of drug.
 5. After establishing access, it is recommended to pre-medicate with acetaminophen and antihistamine 30 minutes prior to infusion, and glucocorticoid 30-60 minutes prior to infusion. Pre-medication recommendations may differ based on the Grade of IRR from the previous infusion(s) and indication.
 6. 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.
 7. Prepare the product:
 - a. 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.
 - b. Withdraw 40 mL (1000 mg) of obinutuzumab from the vial and inject into 250 mL 0.9% sodium chloride bag.
 - c. 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 electronic pump. The product can be administered at a final concentration of 0.4 mg/mL to 4 mg/mL.
 8. Infusion Rates:

Lupus Nephritis (Standard Infusion)		
Dose Number	Dose of Obinutuzumab	Rate of Infusion
1 (Initial Infusion)	1000 mg	Administer at a rate of 50 mg/hr, If tolerated, the rate can be increased in 50 mg/hr increments every 30 minutes to a maximum of 400 mg/hr.
2 (two weeks after dose 1)	1000 mg	Administer at a rate of 100 mg/hr. If tolerated, the rate can
3 (week 24)		

4 (week 26)		be increased at a rate of 100 mg/hr every 30 minutes to a maximum of 400 mg/hr.
5 (6 months after dose 4) and thereafter every 6 months		

Patients who do not experience Grade ≥ 3 infusion related reactions during the previous infusion may receive obinutuzumab over approximately 90 minutes from Dose 2 onwards with premedication.

Lupus Nephritis (90 Minute Infusion)	
Dose Number	Rate
1	See table above
2 and thereafter (if no Grade 3 or higher IRR during previous infusion)	100 mg/hr for 30 minutes, then 900 mg/hr for 60 minutes. If an IRR of Grade 1-2 with ongoing symptoms or a Grade 3 or higher IRR occurs during the previous approximately 90-minute infusion, administer infusion at the standard infusion rate

ANCA-Associated Vasculitis Infusion			
Day of treatment cycle		Dose of Obinutuzumab	Rate of Infusion
Cycle 1 (Induction)	Day 1	1000 mg	Administer at a rate of 50 mg/hr. The rate of infusion can be escalated in 50 mg/hr increments every 30 minutes to a maximum of 400 mg/hr.
	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		

- a. Begin infusion within 4 hours of preparation per current USP Immediate-Use Guidelines
- b. For first dose obinutuzumab at home, administer 250 mL 0.9% sodium chloride hydration concurrently with obinutuzumab with Y-site connector via flow regulator or gravity tubing during the entire duration of the infusion. Fluid administration may be discontinued when obinutuzumab infusion is complete.
- c. Monitor patient and vital signs periodically during the infusion and for 30 minutes after the completion of the infusion per CarePathRx Nursing Best Practice Administration Guidelines

VI. CLINICAL MONITORING

A. Prior to therapy:

1. HBV screening
2. CBC with differential
3. CMP
4. Pregnancy status
5. Ensure patient is up to date on vaccines per CDC guidelines.

B. During therapy:

1. Assessment of signs/symptoms of adverse effects:
2. Hypersensitivity reactions
3. Hepatitis B virus reactivation
4. Tumor lysis syndrome
5. Active infection
6. Blood dyscrasias – thrombocytopenia, neutropenia, signs/symptoms of bleeding
7. Progressive Multifocal Leukoencephalopathy (PML) - focal neurologic deficits, which may present as hemiparesis, visual field deficits, cognitive impairment, aphasia, ataxia, and/or cranial nerve deficits
8. Hypotension (especially if on other medications that lower blood pressure)
9. Common adverse reactions ($\geq 5\%$ lupus nephritis patients in clinical trials): upper respiratory tract infection, COVID-19, urinary tract infection, bronchitis, pneumonia, infusion-related reactions, and neutropenia
10. 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.
11. Labs:
 - a. CBC with differential regularly; if DIC suspected: coagulation parameters and platelet counts
 - b. CMP periodically throughout therapy
 - c. LFTs 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.

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APPENDIX A: ANAPHYLAXIS KIT INSTRUCTIONS

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

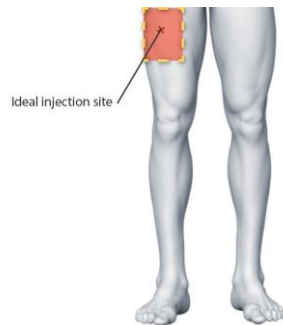
1. Remove 1 of each item

- 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 **hold 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.