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Ocrelizumab (Ocrevus) for Home Infusion Therapy and Ocrelizumab and Hyaluronidase-ocsq (Ocrevus Zunovo) for Home Subcutaneous Infusion Clinical Guideline

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I. BACKGROUND

Ocrelizumab (Ocrevus) is a recombinant humanized monoclonal antibody used for the treatment of relapsing or primary progressive forms of multiple sclerosis (MS) in adult patients. Ocrelizumab binds to CD-20, a cell surface antigen on pre- B and mature B lymphocytes which results in antibody dependent cellular cytotoxicity and complement-mediated lysis. Maintenance IV dosing is 600 mg via intravenous (IV) infusion every 6 months. Ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo) is a subcutaneous infusion that was approved in September 2024. Similar to the original ocrelizumab formulation, the subcutaneous infusion is also approved for relapsing or primary progressive forms of MS in adult patients. The following outlines the procedures for servicing patients in need of outpatient ocrelizumab home intravenous and subcutaneous 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 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
 - 5. Recent baseline CBC with differential
- C. Physician orders for ocrelizumab must include:
 - 1. Drug and dose
 - 2. Route of administration
 - 3. Frequency of administration
 - 4. Emergency medications per protocol

5. Pre-medication orders for Ocrelizumab IV:
 - a. Methylprednisolone 100 mg IV (or equivalent corticosteroid)
 - b. Antihistamine (ex: diphenhydramine)
 - c. The addition of an antipyretic (ex: acetaminophen) may also be considered
 6. Pre-medication orders for Ocrelizumab and Hyaluronidase subcutaneous infusion:
 - a. Dexamethasone 20 mg by mouth (or an equivalent corticosteroid)
 - b. Antihistamine (ex: desloratidine)
 - c. The addition of an antipyretic (ex: acetaminophen) may also be considered
 7. Order for concurrent 250 mL 0.9% sodium chloride IV hydration if approved for first dose at home
 8. Line care protocol
 9. Routine lab monitoring, if applicable
- D. Baseline labs prior to starting therapy
1. Patients must have a Hepatitis B virus (HBV) screening. Ocrelizumab is contraindicated in patients with active HBV.
 2. Prior to initiating ocrelizumab, patients should have quantitative serum immunoglobulins drawn. Patients with low serum immunoglobulins should consult an immunology expert prior to initiating ocrelizumab.
 3. Obtain serum aminotransferases (AST, ALT), alkaline phosphatase, and bilirubin levels
 4. Recent CBC with differential
- E. Ensure patients are up to date on vaccinations. Administer live or live-attenuated immunizations at least 4 weeks prior to therapy initiation, and non-live vaccines at least 2 weeks prior to therapy initiation.
- F. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See Appendix A and Appendix B (Nursing CarepathRx policy on *Management of Allergic/Anaphylactic Reactions*).

III. PHARMACOLOGIC OVERVIEW

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

A. Indications

1. Relapsing forms of multiple sclerosis including clinically isolated syndrome, relapsing-remitting in adults
2. Primary progressive multiple sclerosis in adults

B. Dosing

1. Ocrelizumab IV:

- a. Initial dosing: 300 mg IV, followed by a second 300 mg IV dose two weeks later
 - b. Subsequent dosing: 600 mg IV every 6 months
 2. Ocrelizumab and hyaluronidase subcutaneous:
 - a. 920 mg of ocrelizumab and 23,000 units of hyaluronidase administered as a single 23 mL subcutaneous infusion every 6 months
- C. Dose Adjustments
1. No dose adjustments for renal or hepatic impairment
 2. Missed dose: Give next dose as soon as possible. Reset the dose schedule to administer the sequential dose 6 months after the missed dose. Doses must be separated by at least 5 months.
- D. Duration: Therapy duration depends on patient response and adverse reactions.
- E. Contraindications
1. Active hepatitis B virus infection
 2. History of life-threatening infusion reaction to ocrelizumab
 3. History of hypersensitivity to hyaluronidase
- F. Warnings and Precautions
1. Ocrelizumab IV only:
 - a. **Infusion related reactions:** ocrelizumab can cause infusion reactions, which can include pruritus, rash, urticaria, erythema, bronchospasm, throat irritation, oropharyngeal pain, dyspnea, pharyngeal or laryngeal edema, flushing, hypotension, pyrexia, fatigue, headache, dizziness, nausea, tachycardia, and anaphylaxis. In multiple sclerosis (MS) clinical trials, the incidence of infusion reactions in ocrelizumab-treated patients [who received methylprednisolone (or an equivalent steroid) and possibly other pre-medication to reduce the risk of infusion reactions prior to each infusion] was 34 to 40%, with the highest incidence with the first infusion. There were no fatal infusion reactions, but 0.3% of ocrelizumab-treated MS patients experienced infusion reactions that were serious, some requiring hospitalization. Observe patients treated with ocrelizumab for infusion reactions during the infusion and for at least one hour after completion of the infusion. Inform patients that infusion reactions can occur up to 24 hours after the infusion. Administer pre-medication (e.g., methylprednisolone or an equivalent corticosteroid, and an antihistamine) to reduce the frequency and severity of infusion reactions. The addition of an antipyretic (e.g., acetaminophen) may also be considered.
 2. Ocrelizumab and hyaluronidase subcutaneous:
 - a. **Injection site reactions:** Common symptoms of local injection reactions included erythema, pain, swelling, and pruritis. Common symptoms of systemic injection reactions reported by patients were headache and nausea. 49% of patients experienced an injection reaction with the first injection during the active open-label controlled trial. Monitor patients during and after the subcutaneous infusion for injection reactions. Inform patients that injection reactions can occur during and within 24 hours after the injection.

3. Both ocrelizumab IV and ocrelizumab/hyaluronidase subcutaneous:

- a. Infections:** A higher proportion of ocrelizumab-treated patients experienced infections compared to patients taking interferon beta-1a or placebo. Ocrelizumab increased the risk for upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes-related infections. Ocrelizumab was not associated with an increased risk of serious infections in MS patients. Delay ocrelizumab administration in patients with an active infection until the infection is resolved.
- 1) **Herpes-**In active controlled clinical trials, herpes infections were reported more frequently in ocrelizumab treated patients than in interferon-beta-1a. Infections were mild to moderate in severity. Serious cases of herpes infections (ex: encephalitis, meningitis, intraocular infections) have been reported in post marketing setting. If serious herpes infections occur, ocrelizumab should be discontinued or withheld until the infection is resolved.
 - 2) **Hepatitis B Virus Reactivation-**Hepatitis B reactivation has been reported in MS patients treated with ocrelizumab in the post marketing setting. Fulminant hepatitis, hepatic failure, and death caused by HBV reactivation have occurred in patients treated with anti-CD20 antibodies. Perform HBV screening in all patients before initiation of treatment with ocrelizumab. Do not administer ocrelizumab to patients with active HBV confirmed by positive results for HBsAg and anti-HB tests. For patients who are negative for surface antigen [HBsAg] and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult liver disease experts before starting and during treatment.
- b. Progressive Multifocal Leukoencephalopathy (PML):** Cases of progressive multifocal leukoencephalopathy (PML) has been reported in patients with MS treated with ocrelizumab in the post marketing setting. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. PML has occurred in ocrelizumab-treated patients who had not been treated previously with natalizumab (which has a known association with PML), were not taking any immunosuppressive or immunomodulatory medications associated with the risk of PML prior to or concomitantly with ocrelizumab and did not have any known ongoing systemic medical conditions resulting in compromised immune system function. JCV infection resulting in PML has also been observed in patients treated with other anti-CD20 antibodies and other MS therapies. At the first sign or symptom suggestive of PML, withhold ocrelizumab and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. MRI findings may be apparent before clinical signs or symptoms. Cases of PML, diagnosed based on MRI findings and the detection of JCV DNA in the cerebrospinal fluid in the absence of clinical signs or symptoms specific to PML, have been reported in patients treated with other MS medications associated with PML. Many of these patients subsequently became symptomatic with PML. Therefore, monitoring with MRI for signs that may be consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present. Following discontinuation of another MS medication associated with PML, lower PML-related mortality and morbidity have been reported in patients who were initially asymptomatic at diagnosis compared to patients who had characteristic clinical signs and symptoms at diagnosis. It is not known whether these differences are due to early detection and discontinuation of MS treatment or

due to differences in disease in these patients. If PML is confirmed, treatment with ocrelizumab should be discontinued.

- c. **Reduction in immunoglobulins:** As expected with any B-cell depleting therapy, decreased immunoglobulin levels are observed with ocrelizumab treatment. The pooled data of ocrelizumab clinical studies (RMS and PPMS) and their open-label extensions (up to approximately 7 years of exposure) have shown an association between decreased levels of immunoglobulin G (IgG<LLN) and increased rates of serious infections. Monitor the levels of quantitative serum immunoglobulins during ocrelizumab treatment and after discontinuation of treatment, until B-cell repletion, and especially in the setting of recurrent serious infections. Consider discontinuing ocrelizumab therapy in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.
- d. **Malignancies:** An increased risk of malignancy with ocrelizumab may exist. In controlled trials, malignancies, including breast cancer, occurred more frequently in ocrelizumab-treated patients. Breast cancer occurred in 6 of 781 females treated with ocrelizumab and none of 668 females treated with interferon-beta-1a or placebo. Patients should follow standard breast cancer screening guidelines.
- e. **Immune-Mediated Colitis:** Immune-mediated colitis, which can present as a severe and acute-onset form of colitis, has been reported in patients receiving ocrelizumab in the post marketing setting. Some cases of colitis were serious, requiring hospitalization, with a few patients requiring surgical intervention. Systemic corticosteroids were required in many of these patients. The time from treatment initiation to onset of symptoms in these cases ranged from a few weeks to years. Monitor patients for immune-mediated colitis during ocrelizumab treatment and evaluate promptly if signs and symptoms that may indicate immune-mediated colitis, such as new or persistent diarrhea or other gastrointestinal signs and symptoms, occur.
- f. **Vaccinations:** Administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of ocrelizumab for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of ocrelizumab for non-live vaccines. Ocrelizumab may interfere with the effectiveness of non-live vaccines. The safety of immunization with live or live-attenuated vaccines following ocrelizumab therapy has not been studied, and vaccination with live-attenuated or live vaccines is not recommended during treatment and until B cell repletion.
- g. **Liver injury:** Significant liver injury, without findings of viral hepatitis, has been reported post marketing in patients treated with anti-CD20 B-cell depleting therapies, including ocrelizumab. Signs of liver injury, including markedly elevated serum hepatic enzymes with elevated total bilirubin, have occurred from weeks to months after administration. Patients treated with ocrelizumab and ocrelizumab with hyaluronidase have found to have an AST or ALT greater than 3x the upper limit of normal (ULN) with serum total bilirubin greater than 2x ULN are potentially at risk for severe drug-induced liver injury. Obtain LFTs prior to initiating treatment and monitor for signs and symptoms of any hepatic injury during treatment. Draw LFTs (AST, ALT, alkaline phosphatase, and bilirubin) in patients who report symptoms such as worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice. Ocrelizumab therapy should be discontinued if liver injury is present and an alternative etiology is not identified.
- h. **Pregnancy and Lactation:**

- 1) There is a pregnancy exposure registry that monitors pregnancy and fetal/neonatal/infant outcomes in women exposed to ocrelizumab during pregnancy. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-833-872-4370 or visiting www.ocrevuspregnancyregistry.com.
- 2) Risk Summary: ocrelizumab is a humanized monoclonal antibody of immunoglobulin G1 subtype and immunoglobulins are known to cross the placental barrier. There is no adequate data on the developmental risk associated with use of ocrelizumab in pregnant women. However, transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 antibodies during pregnancy. B-cell levels in infants following maternal exposure to ocrelizumab have not been studied in clinical trials. The potential duration of B-cell depletion in such infants, and the impact of B-cell depletion on vaccine safety and effectiveness, is unknown. Following administration of ocrelizumab to pregnant monkeys at doses similar to or greater than those used clinically, increased perinatal mortality, depletion of B-cell populations, renal, bone marrow, and testicular toxicity were observed in the offspring in the absence of maternal toxicity.
- 3) Vaccination of infants born to mothers treated with ocrelizumab during pregnancy: Do not administer live or live-attenuated vaccines to infants born to mother exposed to ocrelizumab during pregnancy before confirming the recovery of B cell counts as measured by CD19+ B cells. Depleted B cells in these infants may increase the risks from live or live attenuated vaccinations. Non-live vaccines may be administered as indicated prior to recovery from B cell depletion. However, consider consulting a specialist to assess if a protective immune response was mounted prior to vaccine administration.
- 4) Lactation: There is no data on the presence of ocrelizumab in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. Ocrelizumab was excreted in the milk of ocrelizumab-treated monkeys. Human IgG is excreted in human milk, and the potential for absorption of ocrelizumab to lead to B-cell depletion in the infant is unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ocrelizumab and any potential adverse effects on the breastfed infant from ocrelizumab or from the underlying maternal condition.

G. Pharmacokinetics

1. Volume of distribution: 2.78 Liters
2. Metabolism: cleared by catabolism and degraded by proteolytic enzymes
3. Elimination half-life: 26 days (IV) and 20 days (subcutaneous).

H. Adverse Reactions

1. Infection of skin and/or subcutaneous tissue (14%)
2. Lower respiratory tract infection (8-10%)
3. Upper respiratory infection (40-49%)
4. Diarrhea (6%)
5. Colitis (reported cases)
6. Reactivation of hepatitis (reported cases in post marketing)
7. Herpes virus infection (5-6%)
8. Progressive Multifocal leukoencephalopathy (reported cases in post marketing)
9. Peripheral edema (6%)
10. Infusion reaction with IV formulation (34-40%)

11. Injection site reactions with subcutaneous formulation (49% with first dose, and 31-43% with subsequent doses)

I. Drug Interactions

1. The concomitant use of ocrelizumab and other immune-modulating or immunosuppressive therapies, including immunosuppressant doses of corticosteroids, is expected to increase the risk of immunosuppression. Consider the risk of additive immune system effects when co-administering immunosuppressive therapies with ocrelizumab. When switching from drugs with prolonged immune effects, such as daclizumab, fingolimod, natalizumab, teriflunomide, or mitoxantrone, consider the duration and mode of action of these drugs because of additive immunosuppressive effects when initiating ocrelizumab.
2. The safety and effectiveness of live or live-attenuated vaccines administered concomitantly with ocrelizumab have not been assessed.
3. Consult interaction database for patient specific assessment

IV. ADMINISTRATIVE GUIDELINES

- A. Administration: IV and subcutaneous infusions should be given immediately after reconstitution, dilution, and preparation. Begin IV or subcutaneous infusion within 4 hours of preparation per current USP Immediate-Use Guidelines.
- B. Use **in-line or add-on 0.2-micron low protein-binding filter** for ocrelizumab IV infusion.
- C. Do not co-administer with other products in the same IV line.

V. NURSING PROCEDURE

- A. Supplies for ocrelizumab infusion 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 3/4")
 - 3) Extension set 8" with needless connector
 - b. Port access supplies for patients with a port
 - 1) Port needle (ex. 22 Gauge x 3/4 to 1" safe step)
 - 2) Needless connector
 - 3) Central line dressing change kit
 5. IV pole
 6. Syringes for home mix (20-35 mL) with needles (20 G x 1")
 7. Ambulatory pump tubing **with 0.2-micron filter**
 8. Pole mounted ambulatory pump
 9. Batteries for ambulatory pump (Ex: 9 Volt Duracell battery or 4 Double A batteries)

10. Battery change procedure teaching sheet
11. Continuous delivery mode teaching sheet
12. Pump return box
13. 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. Ocrelizumab vial(s)
2. 250 or 500 mL 0.9% Sodium chloride stock bag
3. Pre-medications- IV methylprednisolone or equivalent corticosteroid; antihistamine such as diphenhydramine; antipyretic such as acetaminophen.
4. 250 mL 0.9% sodium chloride bag (for first dose at home)
5. Standard flushes per protocol

C. Supplies for ocrelizumab and hyaluronidase subcutaneous infusion may include but are not limited to:

1. Alcohol swabs
2. Gloves
3. Tape
4. 26 G, 12 mm single-needle high flow needle set
5. F120 Precision Flow Rate Tubing
6. Syringe (60 mL) with needle (20G x 1")
7. Sharps container
8. Freedom 60 Syringe pump, or other appropriate syringe pump
9. Pump return box

D. Prescription items:

1. Vial of ocrelizumab and hyaluronidase
2. Pre-medications- dexamethasone or equivalent corticosteroid; antihistamine such as desloratidine; antipyretic such as acetaminophen.

E. How Supplied:

1. Ocrelizumab IV injection is a preservative-free, sterile, clear or slightly opalescent, and colorless to pale brown solution supplied as a carton containing one 300 mg/10 mL (30 mg/mL) single-dose vial (NDC 50242-150-01).
2. Ocrelizumab and hyaluronidase injection for subcutaneous use is a sterile, preservative-free, clear to slightly opalescent, and colorless to pale brown solution supplied as a carton. The single dose vial contains 920 mg of ocrelizumab and 23,000 units of hyaluronidase in 23 mL (40 mg and 1,000 units/mL) in each vial (NDC 50242-554-01).

F. Storage: Store both ocrelizumab vials and ocrelizumab/hyaluronidase vials at 2°C to 8°C (36°F to 46°F) in the outer carton to protect from light. Do not freeze or shake.

G. Compatibility:

1. Ocrelizumab IV: Compatible in 0.9% Sodium Chloride Injection

2. No incompatibilities between ocrelizumab IV and polyvinyl chloride (PVC) or polyolefin (PO) bags and intravenous (IV) administration sets have been observed.
3. Ocrelizumab and hyaluronidase is compatible with polypropylene (PP), polycarbonate (PC), polyethylene (PE), stainless steel (SS), polyvinylchloride (PVC), and polyurethane (PUR).

H. Procedures (ocrelizumab IV)

1. Explain the reasoning for visit and use of ocrelizumab.
2. Don gloves.
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication.
4. Establish venous access prior to preparation of drug.
5. Counsel patient on warnings, precautions, and potential side effects including but not limited to infusion related reactions, infections, PML, and diarrhea.
6. Administer pre-medications including IV methylprednisolone (or equivalent) and an antihistamine 30-60 minutes prior to starting the ocrelizumab infusion.
7. Prepare ocrelizumab infusion:
 - a. Visually inspect for particulate matter and discoloration prior to administration. Do not use the solution if discolored or if the solution contains discrete foreign particulate matter
 - b. Withdraw 300 mg (10mL) of ocrelizumab from 1 vial or 600 mg (20 mL) of ocrelizumab from 2 vials depending on the dose.
 - c. Inject 300 mg dose in to a 250 mL 0.9% normal saline bag. Inject 600 mg dose in to a 500 mL 0.9% normal saline bag. Invert gently to mix. Do not shake.
 - d. Infuse via pole mounted ambulatory infusion pump

8. Infusion Rates

Table 1 Recommended Dose, Infusion Rate, and Infusion Duration for RMS and PPMS

		Amount and Volume ¹	Infusion Rate and Duration ³
Initial Dose (two infusions)	Infusion 1	300 mg in 250 mL	• Start at 30 mL per hour • Increase by 30 mL per hour every 30 minutes
	Infusion 2 (2 weeks later)	300 mg in 250 mL	• Maximum: 180 mL per hour • Duration: 2.5 hours or longer
Subsequent Doses (one infusion) every 6 months ²	Option 1 Infusion of approximately 3.5 hours duration ³	600 mg in 500 mL	• Start at 40 mL per hour • Increase by 40 mL per hour every 30 minutes • Maximum: 200 mL per hour • Duration: 3.5 hours or longer
	OR		
	Option 2 (If no prior serious infusion reaction with any previous OCREVUS infusion) ⁴ Infusion of approximately 2 hours duration ³	600 mg in 500 mL	• Start at 100 mL per hour for the first 15 minutes • Increase to 200 mL per hour for the next 15 minutes • Increase to 250 mL per hour for the next 30 minutes • Increase to 300 mL per hour for the remaining 60 minutes - Duration: 2 hours or longer

9. For first dose of ocrelizumab IV at home, administer 250 mL 0.9% sodium chloride hydration

concurrently with ocrelizumab with Y-site connector via flow regulator or gravity tubing during the entire duration of the infusion. Fluid administration may be discontinued when ocrelizumab infusion is complete.

10. Post infusion monitoring: Monitor patient and vital signs periodically during the infusion and **1 hour** after the infusion is complete.

I. Procedures for ocrelizumab and hyaluronidase subcutaneous infusion

1. Explain the reasoning for visit and use of ocrelizumab and hyaluronidase
2. Don gloves
3. Assess for signs and symptoms of infection prior to preparation of the medication.
4. Counsel the patient on warnings, precautions, and potential side effects including but not limited to injection site reactions, infections, PML, headache, and diarrhea.
5. Administer pre-medications including PO dexamethasone (or equivalent) and an antihistamine 30-60 minutes prior to administration of ocrelizumab and hyaluronidase.
6. Prepare ocrelizumab and hyaluronidase:
 - a. Remove ocrelizumab and hyaluronidase vial from the fridge
 - b. Withdraw entire contents of ocrelizumab/hyaluronidase solution from the vial with a 30 mL syringe and transfer needle.
 - c. Remove the transfer needle and replace it with a subcutaneous infusion set and F120 tubing. The infusion set priming volume should NOT exceed 0.8 mL. Prime the infusion set with the drug product solution to eliminate the air in the infusion line and stop before the fluid reaches the needle.
 - d. Ensure the syringe contains exactly 23 mL of drug product solution after priming and expelling any excess volume in the syringe.
 - e. Administer immediately to avoid needle clogging. Do not store the prepared syringe that has been attached to the already primed subcutaneous infusion set.
7. Infusion:
 - a. The recommended injection site is the abdomen, except for 2 inches around the navel. Do not administer injections into areas where the skin is red, bruised, tender, hard, or areas where there are moles or scars.
 - b. Administer 23 mL of ocrelizumab and hyaluronidase subcutaneously in the abdomen over approximately 10 minutes. With F120 tubing and 26 G x 12 mm subcutaneous needle set the infusion should run over 11.5 minutes.
8. Post infusion monitoring:
 - a. Monitor patient and vital signs periodically during administration.
 - b. With the first ocrelizumab subcutaneous infusion, monitor patient for **1 hour** after administration is complete.
 - c. For subsequent subcutaneous infusions, monitor the patient for 30 minutes post administration per CarePathRx Nursing Best Practice Administration Guidelines.

VI. CLINICAL MONITORING

A. Prior to therapy

1. Baseline labs prior to starting therapy including baseline CBC with differential
2. Serum aminotransferases (AST, ALT), alkaline phosphatase, and bilirubin levels
3. Serum immunoglobulins
4. Hepatitis B Virus Screening
5. Up to date on vaccinations

B. During therapy

1. Assessment of signs and symptoms of adverse effects
2. Update on previous infusion and if patient experienced and infusion or injection site reaction. Infusion reactions can include: Pruritis, rash, bronchospasm, throat irritation, oropharyngeal pain, dyspnea, pharyngeal or laryngeal edema, flushing, hypotension, headache, dizziness, nausea, or tachycardia. Injection site reactions include erythema, pruritis, pain, and swelling. Inform patients that infusion and injection site reactions can occur up to 24 hours after the infusion.
3. Monitor relapse of disease and disability progression.
4. Prior to every infusion, monitor for any signs/symptoms of infection. Determine whether patient is experiencing an active infection. Delay ocrelizumab infusion if patient has an active infection and re-start when the infection is resolved.
5. Monitor for signs and symptoms of liver injury including worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice.
6. Ocrelizumab may also cause an increased risk of malignancies including breast cancer. Patients should follow standard cancer screening guidelines.
7. Women of child-bearing potential should use contraception while receiving ocrelizumab and for 6 months after the last infusion.
8. Ocrelizumab decreased immunoglobulin levels and neutrophil counts in clinical trials. Monitor Immunoglobulin levels and CBC as ordered by MD.

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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

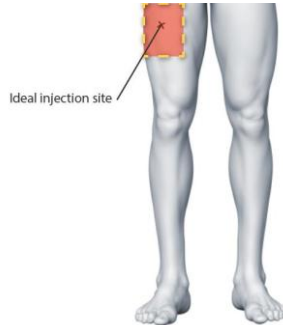
1. Remove 1 of each item
 - a. 1 -syringe
 - b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
 - c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
 - d. 1 ampule of epinephrine

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.

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.

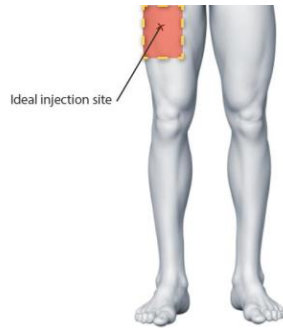
7. Remove the needle from the ampule and hold the syringe upright with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**

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.
3. **Push the needle into your leg muscle straight** in at a 90-degree angle.
4. **Inject the medication** by depressing the plunger in a slow and steady motion.
5. **Remove the needle** and wipe the site with the alcohol wipe.

Place all trash in the bag and take it 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.