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Inebilizumab-cdon (Uplizna) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline

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I. BACKGROUND

Uplizna (inebilizumab) is a humanized IgG monoclonal antibody directed against CD19. The precise mechanism by which inebilizumab exerts its therapeutic effects in neuromyelitis optica spectrum disorder (NMOSD) is unknown. It is presumed to involve binding to CD19, a cell surface antigen presents on both immature and mature B lymphocytes. Following cell surface binding to B lymphocytes, inebilizumab results in antibody-dependent cellular cytotoxicity. Inebilizumab is indicated for the treatment of NMOSD in adult patients who are anti-aquaporin-4 (AQP4) antibody positive, generalized myasthenia gravis (gMG) who are acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive, and for adult patients with Immunoglobulin G4-related disease (IgG4-RD). The following outlines the procedures for servicing patients in need of outpatient intravenous inebilizumab infusions.

II. PATIENT ACCEPTANCE CRITERIA

- A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.
- B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:
 - 1. Prescriber preference
 - 2. Allergy profile
 - 3. Age
 - 4. Other relevant social and/or medical history
- C. Physician orders for inebilizumab must include:
 - 1. Drug and dose
 - 2. Route of administration
 - 3. Frequency of administration
 - 4. Line care per protocol
 - 5. Emergency medications per protocol
 - 6. Orders for IV corticosteroid, oral (PO) antihistamine, and PO antipyretic or equivalent per guidance from the prescribing information (PI). Refer to PI or administrative guidelines subsection C. for examples, dosing ranges, and pre-medication administration windows.
 - 7. Routine lab monitoring, if applicable

D. Baseline labs or tests prior to starting therapy

1. Tuberculosis screening/test (both active and latent)
2. Hepatitis B virus (HBV) screening
3. Quantitative serum immunoglobulins

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

III. PHARMACOLOGY OVERVIEW

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

A. Indications:

1. Neuromyelitis optica spectrum disorder: adults who are anti-aquaporin-4 (AQP4) antibody positive (NMOSD)
2. Generalized myasthenia gravis (gMG) who are acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive
3. Immunoglobulin G4-Related Disease (IgG4-RD) in adult patients

B. Dosing:

1. Initial: 300 mg IV infusion on day 1, followed by 300 mg IV infusion two weeks later.
2. Maintenance: 300 mg IV infusion every 6 months, starting 6 months after the first 300mg dose

C. Dose Adjustments: No renal or hepatic dose adjustments.

D. Duration: Duration of therapy should be dependent on patient response and adverse reactions.

E. Contraindications:

1. Previous life-threatening reaction to infusion of inebilizumab
2. Active hepatitis B infection
3. Active or untreated latent tuberculosis

F. Warnings and Precautions:

1. **Infusion reactions (including anaphylaxis):** Signs and symptoms include headache, nausea, somnolence, dyspnea, fever, myalgia, rash, and palpitations. In clinical trials evaluating inebilizumab for both of its current indications, infusion reactions were noted to be more common during the first infusion. Administer pre-medications prior to infusion. Other management recommendations depend on the type and severity of the reaction. Permanently discontinue inebilizumab if a life-threatening or disabling infusion reaction occurs. Less severe infusion reactions can be managed by temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

2. **Infections:** Possible increased risk of immunosuppressant effects with other immunosuppressants. Inebilizumab has not been studied in combination with other immunosuppressants. If another immunosuppressant is initiated, consideration should be given to the potential for increased immunosuppressive effects. Delay inebilizumab administration in patients with an active infection until the infection is resolved.
 - a. Hepatitis B virus (HBV) reactivation: Risk of HBV reactivation has been observed with B-cell depleting antibodies. Inebilizumab should not be administered to patients with active hepatitis. Screen patients for HBV before initiation of treatment with inebilizumab.
 - b. Progressive multifocal leukoencephalopathy (PML): PML has been observed in patients treated with B-cell depleting antibodies. Inebilizumab should be held if signs or symptoms of PML are present. PML is an opportunistic viral infection caused by the John Cunningham (JC) virus. It typically only causes infection in immunocompromised patients. No confirmed cases of PML have been reported in patients treated with inebilizumab. However, during one clinical trial, a patient died following the development of brain lesions for which a definitive cause could not be identified. Signs and symptoms of PML include progressive weakness on one side of the body, clumsiness of limbs, vision disturbances, changes in thinking/memory/orientation leading to confusion, and personality changes.
 - c. Tuberculosis (TB): TB risk factors should be evaluated and patients tested for latent TB infection prior to inebilizumab initiation. Anti-TB therapy prior to initiation of inebilizumab should be considered in patients with risk factors and those with a history of latent TB infection with no confirmed treatment course.
3. **Vaccinations:** All necessary vaccinations should be completed at least 4 weeks prior to initiation of inebilizumab therapy. Vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation, until B-cell repletion.
4. **Immunoglobulin levels:** Monitor immunoglobulin levels at the beginning, during, and after discontinuation of treatment until B-cell repletion. Consider discontinuation of inebilizumab if a patient with low immunoglobulin G or M develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with IV immunoglobulins.
5. **Fetal risk:** May cause fetal harm based on animal data. Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other B-cell depleting antibodies during pregnancy. Advise females of reproductive potential of the potential risk to a fetus and counsel to use an effective method of contraception during treatment and for 6 months after stopping inebilizumab.
 - a. Lactation: There is no data on the presence of inebilizumab in human milk, effects of breastfed infants, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for inebilizumab and any potential adverse effects on the breast-fed infant from inebilizumab or from the underlying maternal condition.

G. Pharmacokinetics

1. Volume of distribution (central): 2.95 L; Volume of distribution (peripheral): 2.57 L
2. Metabolism: degraded by proteolytic enzymes widely distributed in the body.
3. Half-life: 18 days
4. Excretion: Total body clearance is 0.19 L/day via first order elimination pathway

H. Adverse Reactions

1. > 10%: Urinary tract infections, decreased neutrophils, lymphocytopenia
2. 1%-10%
 - a. Antibody development
 - b. Influenza infection
 - c. Arthralgia, back pain
 - d. Nasopharyngitis, upper respiratory tract infections
 - e. Headache
 - f. Infusion related reactions
3. Undefined frequency
 - a. Decreased serum immunoglobulins

I. Drug Interactions:

1. Concurrent use of immunosuppressant drugs, including systemic corticosteroids, may increase the risk of infection.
2. Vaccinations with live-attenuated or live vaccines is not recommended during or after treatment with inebilizumab until B-cell repletion.
3. Drug-drug interactions may exist. Consult interaction database for patient specific assessment.

IV. ADMINISTRATIVE GUIDELINES

- A. Administration- IV infusions should be given immediately after dilution. Use within 4 hours of preparation per current USP Immediate-Use Guidelines.
- B. Assess for active infection before each infusion. In case of active infection, delay infusion of inebilizumab until the infection resolves.
- C. Pre-medicate with an antihistamine, antipyretic, and a corticosteroid 30-60 minutes prior to infusion.

Type of Premedication	Route of Administration	Examples (or Equivalent)	Administration Time Prior to UPLIZNA Infusion
corticosteroid	intravenous	methylprednisolone 80 mg to 125 mg	30 minutes
antihistamine	oral	diphenhydramine 25 mg to 50 mg	30 to 60 minutes
antipyretic	oral	acetaminophen 500 mg to 650 mg	30 to 60 minutes

- D. A 0.2 or 0.22 micron in-line low-protein binding filter must be used during administration.
- E. Do not co-administer inebilizumab with other products in the same IV line.

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 (10 mL) with needles (20 G x 1")
7. Sharps container
8. Supplies for a pole mounted ambulatory infusion pump:
 - a. Ambulatory pump tubing with a **0.22**-micron filter
 - b. Pole mounted ambulatory pump
 - c. Batteries for ambulatory pump (Ex: 9 Volt Duracell battery or 4 Double A batteries)
 - d. Battery change procedure teaching sheet
 - e. Continuous delivery mode teaching sheet
 - f. Pump return box

B. Prescription Items:

1. Inebilizumab drug vials
2. Bag of sodium chloride 0.9% for dilution (250mL)
3. Standard flushes per protocol
4. Anaphylaxis kit per protocol
5. Pre-medications (see administrative guidelines subsection C for examples)

C. How Supplied: One carton contains 3 single dose inebilizumab vials. Injection vial: 100mg/10mL (10mg/1mL) as a clear to slightly opalescent, colorless to slightly yellow solution.

D. Storage and Handling

1. Refrigerate at 2°C to 8°C (36°F to 46°F) in original carton to protect from light
2. Do not freeze
3. Do not shake
4. Store vials upright

E. Compatibility

1. Dilution with 0.9% Sodium Chloride
2. No compatibility tests for other intravenous agents currently exist

F. Procedures:

1. Explain the reasoning for visit and use of inebilizumab.
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. Counsel patient on warnings, precautions, and potential side effects including but not limited to: increased risk of infections, and infusion reactions. Counsel females of reproductive potential on risk of fetal harm and need to use effective contraception.
6. Prepare Product
 - a. Visually inspect inebilizumab solution for particulate matter and discoloration. If the solution is cloudy, discolored, or contains discrete particulate matter, do not use and contact the manufacturer. Do not shake the vial
 - b. Withdraw 10 mL of inebilizumab from each of the 3 vials contained in the carton and transfer a total of 30 mL into the 250 mL 0.9% sodium chloride bag.
 - c. Mix diluted solution by gentle inversion. Do not shake the solution. Discard the unused portion remaining in the vials.
7. Infusion Rates
 - a. Prior to the start of the intravenous infusion, the prepared infusion solution should be at room temperature. Infuse with increasing rates to completion, approximately over 90 minutes

Elapsed Time (minutes)	Infusion Rate (mL/hour)
0-30	42
31-60	125
61 to completion	333

8. Post infusion monitoring: Monitor patient and vital signs periodically during the infusion (during rate changes) and 60 minutes after the infusion is complete.

VI. CLINICAL MONITORING

A. Prior to therapy

1. HBV screening
2. Quantitative serum immunoglobulins
3. TB screening (active and latent)
4. Assess for active infection prior to each infusion
5. Confirmation of contraceptive use in female patients of reproductive potential
6. Ensure patient is up to date on all necessary vaccinations prior to start of treatment

B. During therapy

1. Quantitative serum immunoglobulins
2. Signs and symptoms of active TB

3. Monitor for infusion reactions during therapy and for at least 1 hour after infusion
4. Signs and symptoms of infection and PML

C. After discontinuation of therapy

1. Quantitative serum immunoglobulins
2. Signs and symptoms of active TB
3. Signs and symptoms of infection and PML

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

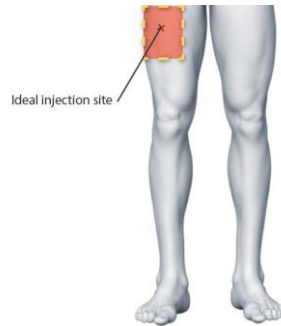
1. Remove 1 of each item
 - a. 1 -syringe
 - b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
 - c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1’')
 - d. 1 ampule of epinephrine

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.