CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

CLINICAL GUIDELINES FOR COVID-19 MONOCLONAL ANTIBODY INJECTIONS

Section: Nursing
Compliance: ACHC Infusion Pharmacy
ACHC Standards:
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Revised:
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I. POLICY STATEMENT

The U.S. Food and Drug Administration has issued an Emergency Use Authorization (EUA) to the emergency use of the unapproved product Evusheld (tixagevimab co-packaged with cilgavimab) for the pre-exposure prophylaxis of coronavirus disease 2019 (COVID-19) in eligible adults and pediatric individuals (12 years of age and older weighing at least 40 kg). This intramuscular (IM) monoclonal antibody preparation is designed to prevent COVID-19 infection in vulnerable and immunocompromised individuals who may not mount an adequate immune response to COVID-19 vaccination or for whom vaccination with any available COVID-19 vaccine is not recommended. Tixagevimab/cilgavimab is not authorized for treatment, post-exposure prophylaxis, or as a substitute for vaccination.

Each drug is a potent, neutralizing IgG1 monoclonal antibody (mAb) directed against the spike protein of SARS-CoV-2. The aim is to block viral attachment and entry into human cells, thus neutralizing the virus, and help prevent COVID-19. The combination monoclonal antibody formulations bind to non-overlapping regions of the receptor binding domain to reduce antibody effector function, minimize risk of antibody-dependent enhancement of disease, and extend antibody half-life. The half-life extension more than triples the durability of its action compared to conventional antibodies with protection lasting at least six months.

II. POLICY

A. All patients referred for tixagevimab/cilgavimab shall meet the clinical admission and EUA criteria.

B. Onboarding information for **pre-exposure prophylaxis of COVID-19** will include:

1. Confirmation that patient was screened by referring institution and meets EUA criteria. Medical conditions may include but are not limited to:
    a. Active treatment for solid tumor and hematologic malignancies

b. Receipt of solid-organ transplant and taking immunosuppressive therapy
c. Receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
d. Moderate or severe primary immunodeficiency
e. Advanced or untreated HIV infection
f. Active treatment with high-dose corticosteroids, alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)

2. Confirmation that patient accepts allocated doses and consents to proceed with treatment.

3. Patients must be screened for any contraindications or precautions, including but not limited to history of platelet or bleeding disorders; heart attack, stroke, or cardiac events; pregnancy; actively breastfeeding.
    a. Patients are eligible a minimum of 14 days after a COVID-19 vaccine
    b. Patients are eligible a minimum of 20 days and symptomatic recovery after a positive COVID-19 test
    c. Patients can receive a COVID-19 vaccine 30 days after Evusheld injection
    d. There is no waiting period following Evusheld and another non-COVID-19 vaccine (i.e. influenza).

4. Demographic and insurance information (if applicable)

C. Physician orders for intramuscular tixagevimab/cilgavimab will include

1. Patient weight (estimate is acceptable)
2. Drug and Dose
3. Route of administration
4. Associated diagnosis (i.e. Z29.1, Z23)
5. Anaphylaxis protocol (required for all patients)

*** Physician prescribing "tixagevimab/cilgavimab per protocol" will meet all these prescription items.**

D. The decision to administer a dose of COVID-19 monoclonal antibody injection in the home 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. Transportation access
3. Allergy profile
4. History of anaphylactic reaction
5. Other relevant social and/or medical history

6. Patient or POA consent to treatment
7. Age ≥12 years and ≥40kg
8. Availability of field nursing

E. Usual dose and administration for **pre-exposure prophylaxis with tixagevimab/cilgavimab:**

1. Dosing for patients ≥12 years ≥ 40 kg and meeting the EUA criteria is 150mg tixagevimab and 150mg cilgavimab administered as two separate consecutive IM injections at different injection sites. No dosage adjustment is recommended in pregnant or lactating individuals, geriatrics, and patients with renal impairment.
2. Repeat dosing is based on available single-dose studies and may be recommended at the clinical judgement of the prescriber if patient requires ongoing protection. While SARS-CoV-2 remains in circulation, patients who are eligible per the EUA may be re-dosed once every 6 months.

F. Treatment protocol for anaphylaxis will be instituted unless otherwise ordered by physician. Refer to Policy NUR012, Appendix A, and Standing Operating Procedure for ***Anaphylaxis Mobile Medical Kit.***

G. Product may be re-labeled with extended shelf-life if authorized by FDA and ASPR

III. PROCEDURES

SUPPLIES AND PROCEDURE FOR INTRAMUSCULAR ADMINISTRATION:

A. Supplies:

1. Alcohol swabs
2. 1 carton EVUSHELD (tixagevimab co-packaged with cilgavimab)
3. 2, 3 cc luer lock syringe
4. 2, 22-gauge safety needles
5. Tamper-proof anaphylaxis mobile medical kit

B. Nursing may don PPE prior to entering the patient's home:

1. N-95 mask
2. Gloves
3. Face shield (if requested)

C. All home participants must wear a mask during the entirety of the nurse's visit.

D. Nursing procedure for administration is as follows:

1. Wash hands

2. Don gloves
3. Counsel patient on warnings, precautions, and potential side effects including but not limited to:
    a. Caution in patients with a history of platelet or bleeding disorder, heart attack, stroke; women who are pregnant or nursing
    b. Injection reactions: pain, bruising, soreness, swelling, or bleeding at the injection site(s)
    c. Allergic reactions: fever, chills, nausea, headache, shortness of breath, change in heart rate or blood pressure, wheezing, swelling of the lips, face, or throat, rash, itching, muscle aches
    d. Cardiac events: pain, pressure, or discomfort in the chest, arms, neck, back, stomach or jaw, shortness of breath, fatigue, nausea

4. Provide the following documentation and review with the patient.
    a. Fact Sheet for Patient, Parents and Caregivers – Emergency Use Authorization (EUA) of Evusheld™ (tixagevimab co-packaged with cilgavimab) for Coronavirus Disease 2019 (COVID-19) (Appendix B).

5. Prepare product: **Tixagevimab 150mg/1.5mL co-packaged with 150mg/1.5mL cilgavimab**
    a. Each Evusheld carton contains two vials, one of each antibody. Each vial contains overfill to allow the withdrawl of 150mg/1.5. ***Two vials needed per dose***
    b. Store unopened vials in refrigerator at 2°-8°C (36°-46°F) in the original carton protected from light. Remove from refrigerated storage before preparation. ***Do not freeze or shake the vials**
    c. Both solutions are clear to opalescent, colorless to slightly yellow. Visually inspect solution for any particulate matter, cloudiness, or discoloration.
    d. Withdraw 1.5mL from one tixagevimab vial (DARK GREY VIAL CAP) into one syringe. Discard unused portion in vial.
    e. Withdraw 1.5mL from one cilgavimab vial (WHITE VIAL CAP) into a second syringe. Discard unused portion in vial.
    f. Product is preservative-free and must be administered immediately.

6. Administration
    a. Administer the two syringes of Evushield consecutively via IM injections at different injection sites in the arm(s), one after the other.
    b. Document administration

IV. MONITORING

A. Monitor patient for one hour via clinical observation. Tracking of vital signs is not required.

B. In case of severe reaction:
    1. Administer emergency medications per protocol and notify physician immediately. Patient

may be transferred to Emergency room or appropriate medical setting if necessary.

C. Adverse events attributed to tixagevimab/cilgavimab must be reported within 7 calendar days of the healthcare provider's awareness of the event.

1. Submit events electronically to FDA Medwatch. The reports should include unique identifiers and "EVUSHELD use for COVID-19 under Emergency Use Authorization (EUA)" under the "Describe Event, Problem, or Product Use/Medication Error" heading.
2. Provide a copy of all FDA MedWatch forms to: AstraZeneca, Fax: 1-866-742-7984.

D. Patient will be discharged from service after completion of injection

REFERENCES:

EVUSHELD [Emergency Use Authorization]. Wilmington, DE: AstraZeneca Pharmaceuticals; 12/2021. Evusheld Healthcare Providers FS 12202021 (fda.gov)

UPMC. Monoclonal Antibody Pre-Exposure Prophylaxis for Immunocompromised Patients. University of Pittsburgh Infonet. Accessed January 14, 2022. Monoclonal Antibody Pre-Exposure Prophylaxis for Immunocompromised Patients (sharepoint.com)

APPENDIX A: ANAPHYLAXIS MEDICAL MOBILE KIT INTRUCTIONS

Anaphylaxis Protocol for COVID-19 Emergency Use Authorization (EUA) Injections Administered in a Home Setting

Nurses administering EVUSHELD™ (tixagevimab/cilgavimab) in the home setting will have access to a tamper-proof Anaphylaxis Medical Mobile Kit. Contents are outlined below.

Population: A complete kit will be present during each home visit. In the event of a significant hypersensitivity reaction or anaphylaxis related to EVUSHELD™, contents will be used per protocol.
Transport, access, and use of this kit by a licensed nurse will be authorized by physicians ordering EUA therapies for pre-exposure prophylaxis of COVID-19.
Indications: Epinephrine should be administered to patients who meet the diagnostic criteria for anaphylaxis. Epinephrine is the drug of choice for anaphylaxis because it can reverse associated hypotension and bronchospasm. There are no absolute contraindications to epinephrine administration in the setting of anaphylaxis.

How supplied:	**Epinephrine administration**:	**Additional Medical Kit Components:**
(2) Acetaminophen 325mg tablets (2) Diphenhydramine 25mg capsules (1) Diphenhydramine 50mg/1mL vial (3) Epinephrine 1mg/mL ampules (1) Methylprednisolone 125mg/2mL vial (1) 0.9% Sodium Chloride (NSS) 500mL bag (3) 1mL TB syringes (3) Filter needles (5 micron) 19 G x 1.5inch (3) Monoject Safety Needles 22 G x 1 inch (2) Syringes, 3 cc, 20G x 1'' (1) Gravity tubing (10) Alcohol swabs	1. Attach filter needle to the 1mL syringe 2. Carefully open ampule of epinephrine 3. Withdraw dose of epinephrine 4. Remove filter needle from syringe and attach 22 G x 1 inch needle 5. Purge any air remaining in syringe 6. Administer dose **intramuscularly** into the anterior to lateral thigh	(2) IV start kits (2) Pairs latex-free gloves (1) Roll of paper tape (1) Extension set with microclave adaptor, 12 in (1) Insyte IV Catheter, 22 G x 1 in (1) Insyte IV Catheter, 24 G x 0.75 in

FOLLOW PHARMCY PROTOCOL FOR MANAGEMENT OF ADULT HYPERSENSITIVTY REACTIONS

*****FOR SEVERE REACTIONS, DO NOT DELAY ADMINISTRATION OF EPINEPHRINE*****

MILD	**MODERATE**	**SEVERE**
For flushing, dizziness, headache, diaphoresis, nausea, or palpitations: Slow drug administration Assess vital signs including Airway, Breathing, Circulation <u>Administer</u> Diphenhydramine **25-50mg PO** **AND/OR** Acetaminophen **650mg PO** **IF NO RELIEF** Infuse NSS at **500-1000mL/hr** If symptoms resolve, may resume infusion at slowed rate and titrate as tolerated	*For chest discomfort, dyspnea, hives, hypotension/hypertension, erythema, fever, or other pronounced symptoms:* **STOP** drug administration Assess vital signs including Airway, Breathing, Circulation <u>Administer</u> Diphenhydramine **25-50mg** IV push Acetaminophen **650mg PO** **IF NO RELIEF** Methylprednisolone **125mg** IV push Infuse NSS at **500-1000mL/hr** Monitor vital signs until WNL If symptoms resolve, may resume infusion at slowed rate and titrate as tolerated	*For bronchospasm, severe hypotension/hypertension, fever with rigors, angioedema, or other potentially life-threatening symptoms:* **STOP** drug administration **CALL 911** Place in supine position and elevate legs Give epinephrine **0.5mg** IM injection (May repeat every 5 minutes x 3 doses if needed) **NSS IV bolus up to 500mL/hr**

APPENDIX B: PATIENT FACT SHEET: TIXAGEVIMAB/CILGAVIMAB

You are being given this Fact Sheet because your healthcare provider believes it is necessary to provide you with EVUSHELD (tixagevimab co-packaged with cilgavimab) for pre-exposure prophylaxis for prevention of coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus. This Fact Sheet contains information to help you understand the potential risks and potential benefits of taking EVUSHELD, which you have received or may receive. The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to make EVUSHELD available during the COVID-19 pandemic (for more details about an EUA please see "What is an Emergency Use Authorization?" at the end of this document).

EVUSHELD is not an FDA-approved medicine in the United States. Read this Fact Sheet for information about EVUSHELD. Talk to your healthcare provider if you have any questions. It is your choice to receive or not receive EVUSHELD.

What is COVID-19? COVID-19 is caused by a virus called a coronavirus. You can get COVID-19 through close contact with another person who has the virus. COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can happen and may cause some of your other medical conditions to become worse. Older people and people of all ages with severe, long-lasting (chronic) medical conditions like heart disease, lung disease, and diabetes, for example, seem to be at higher risk of being hospitalized for COVID-19.

What is EVUSHELD (tixagevimab co-packaged with cilgavimab)? EVUSHELD is an investigational medicine used in adults and adolescents (12 years of age and older who weigh at least 88 pounds [40 kg]) for preexposure prophylaxis for prevention of COVID-19 in persons who are:

- not currently infected with SARS-CoV-2 and who have not had recent known close contact with someone who is infected with SARS-CoV-2 and
    - Who have moderate to severe immune compromise due to a medical condition or
    - have received immunosuppressive medicines or treatments and may not mount an adequate immune response to COVID-19 vaccination or
    - for whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (such as severe allergic reaction) to a COVID-19 vaccine(s) or COVID-19 vaccine ingredient(s).

EVUSHELD is investigational because it is still being studied. There is limited information known about the safety and effectiveness of using EVUSHELD for pre-exposure prophylaxis for prevention of COVID-19. EVUSHELD is not authorized for post-exposure prophylaxis for prevention of COVID-19. The FDA has authorized the emergency use of EVUSHELD for pre-exposure prophylaxis for prevention of COVID-19 under an Emergency Use Authorization (EUA).

What should I tell my healthcare provider before I receive EVUSHELD?

Tell your healthcare provider if you:

• Have any allergies
• Have low numbers of blood platelets (which help blood clotting), a bleeding disorder, or are taking anticoagulants (to prevent blood clots)
• Have had a heart attack or stroke, have other heart problems, or are at high risk of cardiac (heart) events
• Are pregnant or plan to become pregnant
• Are breastfeeding a child
• Have any serious illness
• Are taking any medications (prescription, over the counters, vitamins, or herbal products)

How will I receive EVUSHELD?
EVUSHELD consists of two investigational medicines, tixagevimab and cilgavimab.
• You will receive 1 dose of EVUSHELD, consisting of 2 separate injections (tixagevimab and cilgavimab).
• EVUSHELD will be given to you by your healthcare provider as 2 intramuscular injections. They are usually, given one after the other, 1 into each of your buttocks. After the initial dose, if your healthcare provider determines that you need to receive additional doses of EVUSHELD for ongoing protection, the additional doses would be administered once every 6 months.

Who should generally not take EVUSHELD?
Do not take EVUSHELD if you have had a severe allergic reaction to EVUSHELD or any ingredient in EVUSHELD.

What are the important possible side effects of EVUSHELD? Possible side effects of EVUSHELD are:
• Allergic reactions. Allergic reactions can happen during and after injection of EVUSHELD. Tell your healthcare provider right away if you get any of the following signs and symptoms of allergic reactions: fever, chills, nausea, headache, shortness of breath, low or high blood pressure, rapid or slow heart rate, chest discomfort or pain, weakness, confusion, feeling tired, wheezing, swelling of your lips, face, or throat, rash including hives, itching, muscle aches, dizziness, and sweating. These reactions may be severe or life threatening.
• Cardiac (heart) events: Serious cardiac adverse events have happened, but were not common, in people who received EVUSHELD and in people who did not receive EVUSHELD in the clinical trial studying pre-exposure prophylaxis for prevention of COVID-19. In people with risk factors for cardiac events (including a history of heart attack), more people who received EVUSHELD experienced serious cardiac events than people who did not receive EVUSHELD. It is not known if these events are related to EVUSHELD or underlying medical conditions. Contact your healthcare provider or get medical help right away if you get any symptoms of cardiac events, including pain, pressure, or discomfort in the chest, arms, neck, back, stomach or jaw, as well as shortness of breath, feeling tired or weak (fatigue), feeling sick (nausea), or swelling in your ankles or lower legs. The side effects of getting any medicine by intramuscular injection may include pain, bruising of the skin, soreness, swelling, and possible bleeding or infection at the injection site. These are not all the possible side effects of EVUSHELD. Not a lot of people have been given EVUSHELD. Serious and unexpected side effects may happen. EVUSHELD is still being studied so it is possible that all the risks are not known at this time. It is possible that EVUSHELD may reduce your body's immune response to a COVID-19 vaccine. If you have received a COVID-19 vaccine, you should wait to receive EVUSHELD until at least 2 weeks after COVID-19 vaccination. What other prevention choices are there? Vaccines to prevent COVID-19 are approved or available under Emergency Use Authorization. Use of EVUSHELD does not replace vaccination against COVID-19. For more information about

other medicines authorized for treatment or prevention of COVID-19 go to https://www.fda.gov/emergency-preparednessand-response/mcm-legal-regulatory-and-policy-framework/emergency-useauthorization for more information. It is your choice to receive or not receive EVUSHELD. Should you decide not to receive EVUSHELD, it will not change your standard medical care. EVUSHELD is not authorized for post-exposure prophylaxis of COVID-19.

What if I am pregnant or breastfeeding?
If you are pregnant or breastfeeding, discuss your options and specific situation with your healthcare provider.

How do I report side effects with EVUSHELD?
Contact your healthcare provider if you have any side effects that bother you or do not go away. Report side effects to FDA MedWatch at www.fda.gov/medwatch or call 1-800-FDA-1088 or call AstraZeneca at 1-800-236-9933. Additional Information If you have questions, visit the website or call the telephone number provided below. To access the most recent EVUSHELD Fact Sheets, please scan the QR code provided below. Website Telephone number http://www.evusheld.com 1-800-236-9933

How can I learn more about COVID-19?
- Ask your healthcare provider.
- Visit https://www.cdc.gov/COVID19
- Contact your local or state public health department.

What is an Emergency Use Authorization?
The United States FDA has made EVUSHELD (tixagevimab co-packaged with cilgavimab) available under an emergency access mechanism called an Emergency Use Authorization EUA. The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic. EVUSHELD for pre-exposure prophylaxis for prevention of coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus has not undergone the same type of review as an FDA-approved product. In issuing an EUA under the COVID-19 public health emergency, the FDA has determined, among other things, that based on the total amount of scientific evidence available including data from adequate and well controlled clinical trials, if available, it is reasonable to believe that the product may be effective for diagnosing, treating, or preventing COVID-19, or a serious or life-threatening disease or condition caused by COVID-19; that the known and potential benefits of the product, when used to diagnose, treat, or prevent such disease or condition, outweigh the known and potential risks of such product; and that there are no adequate, approved and available alternatives. All these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic. The EUA for EVUSHELD is in effect for the duration of the COVID-19 declaration justifying emergency use of EVUSHELD, unless terminated or revoked (after which EVUSHELD may no longer be used under the EUA).

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