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PUBLIC HEALTH ADVISORY

To:	All Health Care
From:	Dr. Isaac Benowitz, Maine CDC State Epidemiologist
Subject:	**COVID-19 Pre-exposure Prophylaxis for Patients with Moderate/Severe Immunocompromise**
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COVID-19 Pre-exposure Prophylaxis for Patients with Moderate/Severe Immunocompromise

I. Summary

This health alert provides an update on patient eligibility for EVUSHELD, a long-acting monoclonal antibody that is available under U.S. Food and Drug Administration Emergency Use Authorization for pre-exposure prophylaxis to prevent COVID-19 infection in persons with moderate to severe immunocompromise.

Vaccination for COVID-19 remains the best protection against infection, hospitalization, and death. However, individuals with immunocompromising conditions, or taking certain immunocompromising medications, may be less likely to mount an appropriate immune response to COVID-19 vaccination, leaving them at elevated risk for COVID-19 infection, hospitalization, and death. Many such persons are already at elevated risk for severe disease from COVID-19 due to their existing health conditions. Pre-exposure prophylaxis is now available for certain individuals who have been vaccinated against COVID-19 but remain highly susceptible to this infection and subsequent severe disease.

On December 8, 2021, the U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for EVUSHELD™ (tixagevimab co-packaged with cilgavimab) for the pre-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12+ years and weighing 40+ kg). Tixagevimab and cilgavimab, the active components of EVUSHELD, are neutralizing IgG1 monoclonal antibodies that bind to distinct, non-overlapping epitopes within the receptor binding domain of the spike protein of SARS-CoV-2, the virus that causes COVID-19.

II. Use of EVUSHELD

A. Clinical Trial Data

FDA has determined that, based on the review of the PROVENT clinical trial (NCT04625725), a Phase III randomized, double-blind, placebo-controlled clinical trial, it is reasonable to believe EVUSHELD may be effective as pre-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12+ years of age weighing 40+ kg), and when used under conditions described in FDA's authorization, the known and potential benefits of EVUSHELD outweigh the known and potential risks of treatment.

B. Administration

EVUSHELD may only be used in adults and pediatric individuals (12 years of age and older weighing at least 40 kg):

- Who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2 **and**
    - Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications 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 (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).

C. Limitations on Authorized Use

- EVUSHELD is not authorized for the following uses in individuals:
    - For treatment of COVID-19, **or**
    - For post-exposure prophylaxis of COVID-19 in individuals who have been exposed to someone infected with SARS-CoV-2.
- EVUSHELD may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under State law to prescribe drugs in the therapeutic class to which EVUSHELD belongs (i.e., anti-infectives).
    - Pre-exposure prophylaxis with EVUSHELD is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended. Individuals for whom COVID-19 vaccination is recommended, including individuals with moderate to severe immune compromise who may derive benefit from COVID-19 vaccination, should receive COVID-19 vaccination.
    - For individuals who have received a COVID-19 vaccine, EVUSHELD should be administered at least two weeks after vaccination.
    - The use of EVUSHELD covered by this authorization must be in accordance with the authorized Fact Sheets.

III. Current Eligibility for EVUSHELD in Maine

Maine is taking a stepwise approach to patient eligibility for EVUSHELD. A group from Maine CDC and several healthcare institutions in the state began meeting regularly in December to identify patient conditions that should be prioritized for access to COVID-19 pre-exposure prophylaxis.

Patients with the following medical conditions are currently eligible to receive EVUSHELD:

Category 1 *(currently eligible to receive tixagevimab/cilgavimab therapy)*

- Lung Transplant Recipient (any time frame)
- Small Bowel Recipient (any time frame)
- Receipt of the following immunosuppressive medication within the past 12 months (for any condition, oncology and non-oncology):
    - Anti-thymocyte globulin (ATG)
    - Alemtuzumab
    - Anti-B-Cell Therapy: Rituximab, Ocrelizumab, Ofatumumab
- B-Cell Malignancies, on active treatment (e.g., B-cell lymphomas, chronic lymphocytic leukemia, acute B-cell lymphoblastic leukemia, etc.)
- Multiple Myeloma, on active treatment with two or more agents
- Allogeneic Stem Cell Transplant, within 12 months of Transplant
- Autologous Stem Cell Transplant, within 6 months of Transplant
- Recipient of more than one active Transplant, different Organs (any time frame)
- Acute Myeloid Leukemia under Active Treatment
- Receipt of anti-CD19 or anti-BCMA (CAR)-T-Cell Immunotherapy, within six months of treatment
- Primary or Secondary T-Cell Immunodeficiency, including Severe Combined Immunodeficiency:
    - Agammaglobulinemia (XLA/ARAG)
    - Common Variable Immunodeficiency (CVID) and similar phenotype with T-cell dysfunction
    - Defects of Innate Immunity with predominant susceptibility to Viral Infections (e.g., WHIM Syndrome)
- Additional pediatric conditions (age 12–17 years):
    - Combined immune deficiencies with or without immune dysregulation (e.g., APDS, STAT3 GOF, ALPS)
    - Primary immune regulatory disorders with or without immune deficiency (e.g., APECED, XIAP)
    - High-risk or relapsed acute lymphoblastic leukemia/lymphoblastic lymphoma on intensive therapy (not maintenance therapy)

Category 2 *(currently eligible to receive tixagevimab/cilgavimab therapy)*

- Allogeneic stem cell transplant, more than 12 months since transplant
- Autologous stem cell transplant, more than 6 months since transplant
- Multiple myeloma, on maintenance therapy
- Any solid tumor, on active myelosuppressive chemotherapy
- Any solid organ transplant recipient not otherwise eligible in Category 1
- Other chronic leukemias, on treatment
- *Patients in lower categories with more than one qualifying condition*

Patients with the following medical conditions are NOT YET eligible to receive EVUSHELD, though may become eligible as supply increases:

Category 3 *(not yet eligible to receive tixagevimab/cilgavimab therapy)*

- Active treatment with high-dose corticosteroids (i.e., more than 20 mg prednisone or equivalent per day when administered for two weeks or longer)
- Active treatment with other biologic agents that are immunosuppressive or immunomodulatory, not otherwise listed in Categories 1–2
- Advanced or untreated HIV infection:
    - HIV with CD4 less than 200/mm^3 (if aged less than 14 years, CD4% less than 15%)
    - AIDS-defining illness

Category 4 *(not yet eligible to receive tixagevimab/cilgavimab therapy)*

- Persons 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, e.g., severe allergic reaction to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).
    - Patients with severe allergic reactions to a COVID-19 vaccine include those with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a component of a COVID-19 vaccine or known (diagnosed) allergy to a component of a COVID 19 vaccine, any angioedema affecting the airway (tongue, uvula, or larynx), or diffuse rash which also involves mucosal surfaces (e.g., Stevens-Johnson Syndrome).
        - *Phone consultation with and/or referral to an allergist is strongly recommended for this group as defined by the CDC since history and/or skin testing may allow these patients to receive a vaccine.*
        - NOTE: Severe allergic reactions include anaphylaxis, a progressive life-threatening reaction that can include urticaria (hives) with other symptoms such as wheezing, difficulty breathing, or low blood pressure. Severe allergic reactions do NOT include urticaria beyond the injection site or angioedema (visible swelling) of the lips, facial skin, or skin in other locations. Angioedema of the tongue, uvula, or larynx would NOT be in this category: it is considered a severe allergic reaction.
    - Patients with other non-allergic severe adverse vaccine reactions to a COVID-19 vaccine should undergo review/consultation by an allergist, infectious disease specialist, cardiologist, hematologist/oncologist, neurologist, or other appropriate specialist who is well-informed regarding the state and CDC guidelines to review the possible contraindication. Currently the only recognized contraindication to vaccination is in patients with myocarditis or pericarditis following a dose of mRNA vaccine, pending further study. TTS also a contraindication for Janssen vaccine.

IV. Hemostatic considerations

EVUSHELD is a new combination monoclonal antibody administered as two concomitant IM injections in the gluteal muscle. Maine is experiencing extreme scarcity of blood products to support patients should they have a bleed or hematoma from a deep muscle injection. Thus, strong considerations and judicious clinical discretion is advised for those patients who may be at risk for bleeding from a deep muscle injection.

- Contraindications for administration in patients who otherwise meet EUA eligibility criteria include:
    - **Clinically significant** heritable bleeding disorder or bleeding diathesis despite a normal platelet count.
    - Platelet count **<30,000/uL**.
    - On anticoagulation with warfarin, direct acting oral anticoagulation (DOACs) drug(s), or heparin agents, unless they can be safely held in advance.
    - Dual antiplatelet therapy for stent or other considerations.
- Lastly, please consider as experience with this drug is gained and coincident less stress on the blood supply these parameters will be re-evaluated.

V. Obtaining EVUSHELD For Eligible Patients

Healthcare providers with patients who fit into any of the categories listed above can contact one of the several healthcare systems/facilities in Maine to refer their patient(s) for EVUSHELD treatment. The current list of healthcare systems/facilities currently offering EVUSHELD therapy is available online at https://www.maine.gov/dhhs/mecdc/infectious-disease/epi/airborne/coronavirus/providers.shtml. Information is also available at that website for healthcare systems/healthcare facilities that would like to start getting their own EVUSHELD supply instead of referring patients to other locations.

VI. Recommendations for Healthcare Providers

- Identify all patients who are in currently eligible groups for treatment with EVUSHELD and contact those patients to encourage them to receive this treatment.
- Obtain further information on clinical use of products through NIH's COVID-19 Treatment Guidelines, the Assistant Secretary for Preparedness and Response Public Health Emergency COVID-19 Therapeutics site, and through professional societies such as IDSA's Guidelines on the Management of Patients with COVID-19.
- Continue to encourage COVID-19 vaccination, including booster vaccination.

For More Information

- Fact Sheet for Healthcare Providers: Emergency Use Authorization for EVUSHELD™ (tixagevimab co-packaged with cilgavimab)
- Fact Sheet for Patients, Parents And Caregivers Emergency Use Authorization (EUA) of EVUSHELD™ (tixagevimab co-packaged with cilgavimab) for Coronavirus Disease 2019 (COVID-19)
- Frequently Asked Questions on the Emergency Use Authorization for Evusheld (tixagevimab co-packaged with cilgavimab) for Pre-exposure Prophylaxis (PrEP) of COVID-19
- Omicron Variant: What You Need to Know | CDC
- COVID-19 Treatment Guidelines: What's New
- COVID-19 Treatment Guidelines: Antiviral Therapy
- NIH Statement on Therapies for High-Risk, Nonhospitalized Patients