Medical Directive # 2108003
FOR IMMEDIATE DISTRIBUTION
Date 08/10/2021

OFFICE OF THE MEDICAL DIRECTOR
EMERGENCY PHYSICIANS ADVISORY BOARD

Medical Oversight for the MedStar System

Effective: 08/23/2021 Expiration:

Replaces Medical Directive #: 2108001

Subject: COVID-19 Pandemic – Monoclonal Antibody Administration

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Purpose: The purpose of this directive is to provide guidance for IV administration of monoclonal antibodies, including casirivimab/imdevimab in combination, bamlanivimab/etesevimab in combination, and sotrovimab. The U.S. Food and Drug Administration (FDA) has issued Emergency Use Authorizations (EUA) to permit the emergency use of the unapproved products listed above for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12-years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. This directive may be utilized by Assist and Advanced-credentialed providers who have undergone an OMD-approved training program.

Procedure:

1. Verify and reconcile order from physician or referral with patient
2. Assure documented Positive COVID-19 test and symptoms less than 10-days
3. Ensure patient meets at least one of the criteria for monoclonal antibody administration:
    a. $\geq$ 65-years of age
    b. BMI $\geq$ 25
        i. if 12-17 years of age, BMI $\geq$ 85th percentile
    c. Pregnancy
    d. Chronic kidney disease
    e. Diabetes
    f. Immunosuppressive disease or receiving immunosuppressive treatment
    g. Cardiovascular disease (including congenital heart disease) or hypertension
    h. Chronic lung disease (COPD, asthma, other chronic respiratory disease)
    i. Sickle cell disease/thalassemia
    j. A medical-related technological dependence (trach, gastrostomy, or PPV)
    k. Other high-risk conditions, including but not limited to: cancer, dementia/neurologic conditions, Down Syndrome, HIV infection, liver disease, current or former smoker, organ/stem cell transplant recipient, stroke, substance use disorder
4. Medication preparation per drug-specific Appendix
5. Establish IV per protocol procedure and assure patency
6. Administer per drug-specific Appendix
7. Post-administration
    a. Observe patient for at least 1-hour after infusion is complete.
    b. Obtain vital signs every 30-minutes, and prior to discharge from the infusion location

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Warnings: There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of monoclonal antibodies. The most commonly reported adverse event was nausea. If signs and symptoms of a clinically significant allergic reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

1. Signs and symptoms of infusion related reactions may include:
    1. fever
    2. chills
    3. nausea
    4. myalgia
    5. dizziness
    6. headache
    7. bronchospasm
    8. hypotension
    9. angioedema
    10. throat irritation
    11. rash including urticaria
    12. pruritus
2. If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care per protocol.
3. For non-resolving or progressing adverse reactions, stop infusion and contact the communication center for transport unit and call OLPG.
4. Any reaction listed above occurring during administration or post-administration observation must be documented within the patient record. Items g-l or a life-threatening adverse event must also be reported to OMD via OLPG and self-report.

If you have any questions, do not hesitate to contact me directly.

Veer D. Vithalani MD, FACEP, FAEMS
System Medical Director | Metropolitan Area EMS Authority
Chief Medical Officer | MedStar Mobile Healthcare

References:

- Fact sheet for health care providers: Emergency use authorization (EUA) of REGEN-COV (casirivimab and imdevimab) - https://www.fda.gov/media/145611/download
- Fact sheet for health care providers: Emergency use authorization (EUA) of bamlanivimab and etesevimab - https://www.fda.gov/media/145802/download
- Fact sheet for healthcare providers: Emergency use authorization (EUA) of sotrovimab - https://www.fda.gov/media/149534/download
- People with Certain Medical Conditions: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html
- Underlying Medical Conditions Associated with High Risk for Severe COVID-19: Information for Healthcare Providers: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

Appendix A: Casirivimab/Imdevimab

Medication Preparation

1. Remove casirivimab and imdevimab vials from cold storage and allow to equilibrate to room temperature (approx. 20-mins.) DO NOT EXPOSE TO DIRECT HEAT
2. Inspect for particulate matter and discoloration
3. Using aseptic technique, withdraw 600mg Casirivimab & 600mg of Imdevimab
    a. 10ml of co-formulated, or
    b. 5ml (or two 2.5ml) of each medication
4. Inject into 50mL, 100mL, or 250mL normal saline prefilled fluid bag
5. Gently invert infusion bag by hand approximately 10 times to mix. DO NOT SHAKE
6. Inspect for particulate matter and discoloration
    a. Can be clear to slightly opalescent and colorless to slightly yellow to slightly brown solution
7. If immediate administration is not possible, store diluted casirivimab/imdevimab solution in the refrigerator at 2-8°C (36-46°F) for no more than 36-hours or at room temperature up to 25°C (77°F) for no more than 4-hours. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30-minutes prior to administration.

Medication Administration

1. Gather the recommended materials for infusion:
    a. Polyvinyl chloride (PVC), polyethylene (PE)-lined PVC, or polyurethane (PU) infusion set containing a 0.20 micron in-line polyethersulfone (PES) filter.
2. Attach the infusion set to the IV bag and prime.
    a. Administer the infusion solution via pump or dial-a-flow per the infusion table below
    b. Prepared infusion is not to be administered with any other drug as compatibility is unknown
3. Once infusion is complete, flush the infusion line to ensure delivery of the required dose.
4. Discard unused product, if any
5. Clinically monitor patients during administration.
    a. Pre-administration vital signs, then every 15-minutes and at completion of infusion

Infusion table for Casirivimab/Imdevimab

Size of Prefilled 0.9% Sodium Chloride Infusion Bag used	Maximum Infusion Rate	Minimum Infusion Time
50 mL	180 mL/hr	20-minutes
100 mL	310 mL/hr	21-minutes
250 mL	310 mL/hr	50-minutes

Appendix B: Bamlanivimab/Etesevimab

Medication Preparation

1. Remove one (1) bamlanivimab and two (2) etesevimab vials from cold storage and allow to equilibrate to room temperature (approx. 20-mins.) DO NOT EXPOSE TO DIRECT HEAT
2. Inspect for particulate matter and discoloration
3. Using aseptic technique, withdraw 700mg (20 mL) from one (1) vial of bamlanivimab and 1,400mg (40 mL) from two (2) vials of etesevimab into one (1) 60 mL syringe
4. Inject into 50mL, or 100mL, or 250mL normal saline prefilled fluid bag
5. Gently invert infusion bag by hand approximately 10 times to mix. DO NOT SHAKE
6. Inspect for particulate matter and discoloration
    a. Can be clear to slightly opalescent and colorless to slightly yellow to slightly brown solution
7. If immediate administration is not possible, store the diluted infusion solution for up to 24-hours at refrigerated temperature (2-8°C [36-46°F]) and up to 7-hours at room temperature (20-25°C [68-77°F]) including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 20-minutes prior to administration.

Medication Administration

1. Gather the recommended materials for infusion:
    a. Polyvinyl chloride (PVC), polyethylene (PE)-lined PVC, or polyurethane (PU) infusion set containing a 0.20/0.22 micron in-line polyethersulfone (PES) filter.
2. Attach the infusion set to the IV bag and prime.
    a. Administer the infusion solution via pump or dial-a-flow per the infusion table below
    b. Prepared infusion is not to be administered with any other drug as compatibility is unknown
3. Once infusion is complete, flush the infusion line to ensure delivery of the required dose.
4. Discard unused product, if any
5. Clinically monitor patients during administration.
    a. Pre-administration vital signs, then every 15-minutes and at completion of infusion

Infusion table for Bamlanivimab/Etesevimab

Size of Prefilled 0.9% Sodium Chloride Infusion Bag used	Maximum Infusion Rate	Minimum Infusion Time
50 mL	310 mL/hr	21-minutes
100 mL	310 mL/hr	31-minutes
250 mL	< 50kg – 266 mL/hr > 50kg – 310 mL/hr	< 50kg – 70-minutes > 50kg – 60-minutes

Appendix C: Sotrovimab

Medication Preparation

1. Remove one (1) sotrovimab vial from cold storage and allow to equilibrate to room temperature, protected from light (approx. 15-mins.) DO NOT EXPOSE TO DIRECT HEAT
2. Inspect for particulate matter and discoloration
3. Gently swirl the vial several times before use without creating air bubbles. Do not shake the vial.
4. Using aseptic technique, withdraw 500mg (8ml) from one (1) vial of sotrovimab into a syringe
5. Inject into 100mL normal saline prefilled fluid bag
6. Gently invert infusion bag by hand approximately 3-5 times to mix. DO NOT INVERT
7. Inspect for particulate matter and discoloration
    a. Can be clear to slightly opalescent and colorless to slightly yellow to slightly brown solution
8. If immediate administration is not possible, store the diluted infusion solution for up to 4-hours at room temperature (20-25°C [68-77°F]) or refrigerated up to 24-hours (2-8°C [36-46°F]).

Medication Administration

1. Gather the recommended materials for infusion:
    a. Polyvinylchloride (PVC) or polyolefin (PO) infusion set containing a 0.2 micron in-line polyethersulfone (PES) filter.
2. Attach the infusion set to the IV bag and prime.
3. Administer the infusion solution via pump or dial-a-flow over at least 30-minutes
4. Prepared infusion is not to be administered with any other drug as compatibility is unknown
5. Once infusion is complete, flush the infusion line to ensure delivery of the required dose.
6. Discard unused product, if any
7. Clinically monitor patients during administration.
    a. Pre-administration vital signs, then every 15-minutes and at completion of infusion