NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

NC State Health Director's Statewide Standing Order
for Intravenous Administration of Bamlanivimab/Etesevimab Monoclonal Antibodies
October 29, 2021

Purpose: To meet the goal of administering FDA-Emergency Use Authorization bamlanivimab/etesevimab to treat mild to moderate coronavirus disease, or for post-exposure prophylaxis (PEP) of COVID-19, in patients who are high risk for progression to severe COVID-19 and who meet the criteria set-forth by the Emergency Use Authorization Food and Drug Administration.

Policy: This standing order authorizes any North Carolina healthcare provider, in accordance with the conditions of their licensure and/or scope of practice to include intravenous infusions, or pursuant to orders issued under North Carolina Executive Order 236, or as a covered person under the federal PREP Act functioning as monoclonal antibody providers to administer bamlanivimab/etesevimab authorized by the FDA through an Emergency Use Authorization (EUA) and per conditions of this order.

<table>
<tr><th colspan="3">Bamlanivimab/ Etesevimab Administration</th></tr>
<tr><td>Condition or Situation</td><td colspan="2">Patients aged 12 years and older, weighing at least 40 kg (88.2 lb.), who present requesting and consent to treatment with monoclonal antibodies bamlanivimab/etesevimab for treatment of mild to moderate COVID-19 or for post-exposure prophylaxis to COVID-19, who self-attest to being at high risk for severe COVID-19 disease. Patients should have legal and decisional capacity to consent to treatment with monoclonal antibodies bamlanivimab/etesevimab in accordance with NC GS § 91-21.13 and NC GS § 90-21.5.

Bamlanivimab/etesevimab can only be administered in settings in which healthcare providers have immediate access to medications to treat a severe infusion or hypersensitivity reactions (such as anaphylaxis), and the ability to activate EMS, as necessary and according to local protocol.</td></tr>
<tr><th colspan="3">Assessment Criteria</th></tr>
<tr><td>Subjective</td><td>Treatment of Mild to Moderate COVID-19</td><td>Post-Exposure Prophylaxis of COVID-19</td></tr>
<tr><td></td><td>1. Patient self-attests to positive results of SARS-CoV-2 viral testing AND
2. The patient presents within 10 days of symptom onset of COVID-19.</td><td>1. The patient self-attests that they are not fully vaccinated against COVID-19 or are not expected to mount an adequate immune response to complete COVID-19 vaccination AND
2. The patient self-attests that they are a close contact to an individual infected with COVID-19 or are at high risk of exposure to COVID-19 due to higher occurrence of infection in an institutional setting (for example, in nursing homes and correctional settings).</td></tr>
<tr><td></td><td colspan="2">In addition to meeting one of the above criteria, the patient self-attests to having a condition that would put them at high-risk for progression to severe COVID-19. Refer to the CDC's review of People with Certain Medical Conditions for the most recent</td></tr>
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	guidance on medical conditions that place a person at higher risk for severe illness with COVID-19. High risk conditions may include, but not be limited to: 1. Older age (for example, over the age of 65) 2. Obesity or being overweight (for example, BMI > 25; or if age 12-17, have BMI ≥ 85th percentile for their age and gender based on CDC growth charts) 3. Pregnancy 4. Chronic kidney disease 5. Diabetes 6. Immunosuppressive disease or immunosuppressive treatment 7. Cardiovascular disease (including congenital heart disease) or hypertension 8. Chronic lung diseases (for example, chronic obstructive pulmonary disease, moderate-to-severe asthma, interstitial lung disease, cystic fibrosis, and pulmonary hypertension) 9. Sickle cell disease 10. Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies) 11. Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation unrelated to COVID-19) Patients may self-attest they have another condition or factor that may put them at high risk for progression to severe COVID-19 disease that is not listed above. If the patient presents with another condition or factor that is not listed above and the patient is uncertain if it may put them at high risk for progression to severe COVID-19 disease and therefore cannot self-attest to high risk, consult with the physician or advanced practice provider (APP; nurse practitioner, certified nurse-midwife, or physician assistant) providing clinical supervision of the treatment facility/agency/service. Patient should self-attest that in the two weeks (14 days) preceding infection or exposure to COVID-19, that they have not travelled to, resided in, or had close contact with an infected individual from an area where the frequency of resistant variants to bamlanivimab/etesevimab exceeds 5%. Bamlanivimab/ etesevimab are not authorized for use in areas where the combined frequency of resistant viral variants is greater than 5%. See the FDA's list of Bamlanivimab and Etesevimab Authorized States, Territories & US Jurisdictions. An alternative monoclonal antibody should be used in this circumstance.
Objective	1. The patient is at least 12 years of age or older. 2. The patient weighs at least 40 kg, or 88.2 lb. a. Note whether the patient weighs ≥ 50 kg, or 110.2 lbs, to ensure the appropriate infusion rate is selected.

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Plan of Care	
Actions	1. Review Fact Sheet for Health Care Providers 2. Review agency protocol for assessment and management of anaphylaxis **before** initiating treatment. Appropriate medical treatment and clinical staff able to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration reaction according to agency protocol. 3. Prior to patients receiving bamlanivimab/etesevimab, provide and review the Fact Sheet for Patients, Parents and Caregivers EUA of Bamlanivimab and Etesevimab for COVID-19. 4. Before administering bamlanivimab/etesevimab or participating in any patient care activities, don appropriate personal protective equipment (PPE) per CDC guidelines to protect against the transmission of COVID-19.
Precautions: Patient Monitoring	The patient should be clinically monitored during and after administration of bamlanivimab/etesevimab. After administration is complete, the patient should be monitored for a minimum of 1 hour. During this time, the nurse, EMS personnel, or other individuals who are trained and supervised by clinical staff shall observe for signs and symptoms of a hypersensitivity reaction (anaphylaxis) or infusion related reaction. These may include: 1. Fever 2. Difficulty breathing 3. Reduced oxygen saturation 4. Chills 5. Nausea 6. Arrhythmia (such as atrial fibrillation, tachycardia, or bradycardia) 7. Chest pain or discomfort 8. Weakness 9. Altered mental status 10. Headache 11. Bronchospasm 12. Hypotension 13. Hypertension 14. Angioedema 15. Throat irritation 16. Rash (urticaria) 17. Pruritus 18. Myalgia 19. Vasovagal reaction 20. Dizziness 21. Fatigue 22. Diaphoresis

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<table>
<tr><td></td><td>If the patient is showing signs of anaphylaxis or an infusion/injection related reaction during or after administration; stop treatment, implement medical emergency protocols and immediately notify the physician or APP providing clinical supervision of the treatment facility/agency/service.</td></tr>
<tr><td>Treatment</td><td>Bamlanivimab/ etesevimab may be given by <u>IV infusion</u> ONLY.
1. Prepare 700 mg (1 vial) bamlanivimab and 1400 mg (2 vials) etesevimab according to manufacturer instructions using aseptic technique. 700 mg of bamlanivimab and 1400 mg of etesevimab are added to the same infusion bag and administered together as a single intravenous infusion.
a. For patients weighing at least 40 kg (88.2 lb) but <u>less</u> than 50 kg (110.2 lb), follow the RXWorkflow for Bamlanivimab/Etesevimab for Patients Weighing Less than 50 kg.
b. For patients weighing 50 kg (110.2 lb) or more, follow the RXWorkflow for Bamlanivimab/Etesevimab for Patients Weighing 50 kg or More
2. Gather the recommended materials for infusion:
a. Polyvinyl chloride (PVC), polyethylene (PE)-lined PVC, according to local supply and protocol
b. In-line or add-on 0.2-micron polyethersulfone (PES) filter, according to local supply and protocol
3. Attach the infusion set to the intravenous bag.
4. Prime the infusion set.
5. Administer the entire infusion solution in the bag via pump or gravity, according to local supply and protocol, through an intravenous line containing a sterile, in-line or add-on 0.2-micron PES filter. Due to potential overfill of prefilled saline bags, the entire infusion solution in the bag should be administered to avoid underdosage.
a. Follow local protocol for IV site selection and administration.

Dilution Instructions and Administration Rate for IV Infusion in Patients
Add 1 vial (20 mL) of bamlanivimab and 2 vials of etesevimab (40 mL) and inject all 60 mL into a prefilled 0.9% sodium chloride infusion bag and administer as instructed below.
<table>
<tr><th>Size of Prefilled 0.9% Sodium Chloride Infusion Bag</th><th>Maximum Infusion Rate</th><th>Minimum Infusion Time</th></tr>
<tr><td>50 mL</td><td>310 mL/hr</td><td>21 minutes</td></tr>
<tr><td>100 mL</td><td>310 mL/hr</td><td>31 minutes</td></tr>
<tr><td>150 mL</td><td>310 mL/hr</td><td>41 minutes</td></tr>
<tr><td>250 mL</td><td>266 mL/hr</td><td>*70 minutes OR 60 minutes</td></tr>
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	* in patients weighing **less** than 50 kg (110.2 lb) receiving treatment with the 250 mL prefilled sodium chloride infusion bag, the minimum infusion time must be at least 70 minutes to ensure safe use. 6. The prepared infusion solution should not be administered simultaneously with any other medication. 7. After the infusion is complete, flush the tubing with 0.9% Sodium Chloride. 8. Discard unused product.
Follow-up	1. Provide the patient with COVID-19 Antibody Therapy Discharge Instructions and review it with them. 2. Patients treated with bamlanivimab and etesevimab should continue to use infection precautions and isolate or quarantine according to CDC Criteria for Quarantine and Isolation. 3. Administrators of bamlanivimab and etesevimab should report all medication errors and serious adverse events within 7 days from the onset of the event. This can be found here: http://www.fda.gov/medwatch/report.htm. Please note, all fields should be completed with as much detailed information as possible.
Contraindications for Use of this Order	Do not administer bamlanivimab/ etesevimab monoclonal antibody treatment to patients that: 1. Have previous severe hypersensitivity reaction, such as anaphylaxis, to bamlanivimab/ etesevimab or to any ingredient of bamlanivimab/ etesevimab. 2. Are hospitalized due to COVID-19. 3. Require oxygen therapy due to COVID-19. 4. Require an increase in baseline oxygen flow rate due to COVID-19 for patients on chronic oxygen therapy due to underlying non-COVID-19 related morbidity. 5. Have travelled to, resided in, or had close contact with an infected individual from an area where the frequency of resistant variants to bamlanivimab/ etesevimab exceeds 5% in the two weeks (14 days) prior to presenting for treatment/post-exposure prophylaxis. An alternative monoclonal antibody should be used in this circumstance
Criteria or Circumstances for Notifying the Physician or Advanced Practice Provider (APP)	Notify the physician/APP if: 1. The patient desires treatment or post-exposure prophylaxis with bamlanivimab/ etesevimab but is uncertain if they meet the assessment criteria for use. 2. The patient exhibits signs of a hypersensitivity reaction (anaphylaxis) or an infusion/injection-related reaction. In this instance, stop treatment; initiate emergency medical protocols and notify the physician/ APP providing clinical supervision of the treatment facility/agency/service. 3. Notify the physician/APP from the organization providing clinical supervision of the treatment facility/agency/service at any time there are questions or problems with carrying out this standing order.

Approved by: ___CT Wilson_____ _____ Date approved: __10-29-21_____

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This order is effective immediately upon signing and may be revised or revoked by the State Health Director according to his/her discretion. Legal Authority: Executive Order 236