NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

NC State Health Director's Statewide Standing Order
for Intravenous Administration of Bamlanivimab/ Etesevimab Monoclonal Antibodies
Revised January 5, 2022

Due to the increase in cases of COVID-19 and the emergence of the Omicron variant, there may be logistical or supply constraints that make it impossible to offer the available therapy to all eligible patients, making patient triage necessary. This SO has been revised to provide patient prioritization criteria.

Purpose: To meet the goal of administering FDA-Emergency Use Authorization Bamlanivimab/Etesevimab (administered together) to treat mild to moderate coronavirus disease in adults and pediatric patients, including neonates, 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 245, 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

Bamlanivimab/ Etesevimab Administration	
Condition or Situation	***Attention Providers:** BAM/ETE is **not** an effective treatment against the Omicron variant of COVID-19. BAM/ETE shall only be administered under this standing order in settings that have capability to rule out the Omicron variant (e.g., by S gene Target Failure in the ThermoFisher TaqPath assay) as cause of patient illness **and** can administer treatment within 48 hours of results *Patients of all ages (including neonates who meet the assessment criteria), presenting for treatment, with monoclonal antibodies bamlanivimab/etesevimab, of mild to moderate COVID-19 who self-attest to, or their parent/legal guardian attests on their behalf, being at high risk for severe COVID-19 disease. Patient consent to treatment with monoclonal antibodies bamlanivimab/etesevimab should be obtained 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.
Assessment Criteria	
Subjective	**Treatment of Mild to Moderate COVID-19** 1. Patient self-attests to, or parent/legal guardian attests on their behalf, positive results of SARS-CoV-2 viral testing **AND** 2. The patient presents within 10 days of symptom onset of COVID-19. 3. In addition to the above criteria, the patient self-attests to **ONE** of the following: • Vaccinated individuals who are moderately to severely immunocompromised, who may not mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying

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	conditions. (For examples of immunocompromised conditions, see this link: Moderately or Severely Immunocompromised People) **or** • Unvaccinated individuals aged 65 or older (with or without an underlying condition) **or** • Unvaccinated individuals under age 65 with underlying medical condition that puts them at greatest risk for severe disease. (For examples of medical conditions that increase risk of severe disease, see this link: People with Certain Medical Conditions).
Objective	To ensure the appropriate dose/infusion rate table is selected, note which of the following is true: a. Patient is 18 years of age or older **or** under 18 years weighing at least 40 kg (88.2 lb) (Table 1) b. Patient is under 18 years of age **and** weighs less than 40 kg (88.2lb) (Table 2)
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. 3. Appropriate medical treatment and clinical staff able to manage immediate infusion/allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration reaction according to agency protocol. Must have the ability to activate EMS, as necessary. 4. 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. 5. 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 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.
Treatment	***Bamlanivimab and etesevimab are authorized to be administered together and by <u>IV infusion</u> ONLY.** **<u>General Information for Adult and Pediatric Infusions</u>** 1. Remove bamlanivimab and etesevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake vials. Inspect vials for discoloration, or particulate matter**. 2. Discard any product remaining in the vials after injecting into infusion bag. 3. When preparing infusion solution, gently invert the bag by hand approximately 10 times to mix. **Do not shake.** 4. Prepared infusion solution should not be administered simultaneously with any other medication. 5. If the infusion must be discontinued due to infusion reaction, discard any unused product 6. Follow local protocol for IV site selection and administration. ➢ **<u>Patients 18 years of age or older, and Pediatric patients weighing at least 40 kg (88.2 lb) :</u>** 1. Prepare 700 mg (1 vial) bamlanivimab and 1400 mg (2 vials) etesevimab according to manufacturer instructions using aseptic technique. Vials added to the same infusion bag and administered together as a single intravenous infusion. 2. Attach the infusion set to the intravenous bag. 3. Prime the infusion set. 4. Administer the entire infusion solution in the bag via pump or gravity, (see **Table 1** for Infusion Rate) 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.

Table 1: Dilution and Administration Instructions for Bamlanivimab and Etesevimab for IV Infusion in Adults (≥18 years regardless of weight) and Pediatric Patients (<18 years and weighing at least 40 kg)

Size of Prefilled 0.9% Sodium Chloride Infusion Bag	Maximum Infusion Rate	Minimum Infusion Time
50 mL	310 mL/hr	21 minutes
100 mL	310 mL/hr	31 minutes
150 mL	310 mL/hr	41 minutes
250 mL	310 mL/hr **(Patients weighing at least 50 kg)**	60 minutes
***250 mL**	266 mL/hr **(Patients weighing at least 40kg, but less than 50 kg)**	70 minutes

* in patients weighing at least 40 kg (88.2 lb) but **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.

- **Patients less than 18 years of age, and weighing less than 40 kg:**

1. Withdraw appropriate amounts of bamlanivimab and etesevimab from vials based on body weight and inject into the empty infusion bag or draw into a disposable syringe (see **Table 2** below).
2. Multiple doses of bamlanivimab and etesevimab may be prepared from each product vial.
3. Prepare all infusion bags or syringes at the same time. Appropriately label any prepared doses including the patient weight and dose, and time of preparation to minimize risk of medication errors, particularly in cases where multiple doses are prepared simultaneously.
4. IV bag: Attach the infusion set to the IV bag. Prime the infusion set.
   Administer the entire infusion solution in the bag via pump or gravity over **no less than 16 minutes** (see **Table 2** below). Once infusion is complete, flush the tubing with 0.9% Sodium Chloride to ensure delivery of the required dose.
5. Syringe Pump: Administer the entire contents of the syringe via syringe pump over **no less than16 minutes** (see **Table 2** below). After the entire contents of the syringe have been administered, flush the extension set with 0.9% Sodium Chloride to ensure delivery of the required dose.

Table 2: Dosing, Preparation and Administration Instructions for Undiluted Bamlanivimab and Etesevimab for IV Infusion in Pediatric Patients (<18 years and weighing less than 40 kg)

Body Weight	BAM/ETE dose (mg)	Amount of BAM (as mL)	Amount of ETE (as mL)	Maximum Infusion Rate
>20 kg to <40 kg	350 mg / 700 mg	10 mL	20 mL	1.88 mL/min
>12 kg to <20 kg	175 mg / 350 mg	5 mL	10 mL	0.94 mL/min
>11 kg to 12 kg	138 mg / 276 mg	3.9 mL	7.9 mL	0.74 mL/min
>10 kg to 11 kg	126 mg / 252 mg	3.6 mL	7.2 mL	0.68 mL/min
>9 kg to 10 kg	114 mg / 228 mg	3.3 mL	6.5 mL	0.61 mL/min
>8 kg to 9 kg	102 mg / 204 mg	2.9 mL	5.8 mL	0.54 mL/min
>7 kg to 8 kg	90 mg / 180 mg	2.6 mL	5.1 mL	0.48 mL/min
>6 kg to 7 kg	78 mg / 156 mg	2.2 mL	4.5 mL	0.42 mL/min
>5 kg to 6 kg	66 mg/ 132 mg	1.9 mL	3.8 mL	0.36 mL/min
>4 kg to 5kg	54 mg / 108 mg	1.5 mL	3.1 mL	0.29 mL/min
>3 kg to 4 kg	42 mg / 84 mg	1.2 mL	2.4 mL	0.23 mL/min
>2 kg to 3 kg	30 mg / 60 mg	0.9 mL	1.7 mL	0.16 mL/min
>1.5 kg to 2 kg	21mg / 42 mg	0.6 mL	1.2 mL	0.11 mL/min
>1 kg to 1.5 kg	15mg / 30 mg	0.3 mL	0.9 mL	0.08 mL/min

*****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. (See Precautions: Patient Monitoring section)**

Follow-up

1. Provide the patient with COVID-19 Antibody Therapy Discharge Instructions and review it with them.
2. Patients treated with bamlanivimab / etesevimab should continue to use infection precautions and isolate or quarantine according to CDC Criteria for Quarantine and Isolation.

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	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. Age 2 or older and 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.
Criteria or Circumstances for Notifying the Physician or Advanced Practice Provider (APP)	Notify the physician/APP if: 1. The patient desires treatment 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.

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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 245