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TO: **YNHHS MEDICAL STAFF**

FROM: **YNHHS ANTIMICROBIAL STEWARDSHIP COMMITTEE**

SUBJECT: **Update on Outpatient Monoclonal Antibody Therapy for COVID-19**

DATE: **JUNE 25, 2021**

Situation:
Since the incidence of the Beta (B.1.351, originally identified in South African) and Gamma (P.1, originally identified in Brazil) variants now exceed 11% in the US, HHS now has paused the distribution of bamlanivimab/etesivimab for the treatment of mild to moderate COVID-19 in outpatients with risk factors for severe disease and/or hospitalization. In lieu of bamlanivimab/etesevimab, casirivimab/imdesivimab is now recommended as a monoclonal antibody therapy for this patient population.[1]

Background:
Although both agents, bamlanivimab/etesevimab and casirivimab/imdevimab, are monoclonal antibodies directed against the spike protein of SARS CoV-2, their neutralizing ability is affected by the COVID-19 variants.
Below is a table illustrating the differences in an *in-vitro* model of antibody activity against SARS CoV-2 stratified by variant.[2,3]

Lineage with Spike Protein Substitution	Key Substitution Tested	Bamlanivimab/Etesevimab Fold Reduction in Susceptibility	Casirivimab/Imdevimab Fold Reduction in Susceptibility
B.1.1.7 (UK origin)	N501Y	No change	No change
B.1.351 (South African origin)	K417N+E484K+N501Y	215	No change
P.1 (Brazil origin)	K417T+E484K+N501Y	>46	No change
B.1.427/B.1.429 (California origin)	L452R	9	No change
B.1.526 (New York Origin)	E484K	31	No change

However, it is not known how the results of the *in-vitro* model above correlates with clinical outcomes.

Of note, the most recent data from Connecticut indicates that the incidence of the Beta and Gamma variants has been low at 0% and 4.5%, respectively.[4]

Assessment:
Based on the latest guidance detailed above, casirivimab/imdevimab will be the monoclonal therapy offered at YNHHS for outpatients with mild to moderate COVID-19 who are at high risk for severe disease or hospitalization.

Recommendations:
YNHHS will no longer administer bamlanivimab/etesevimab and will only administer casirivimab/imdesivimab for the outpatient treatment of mild to moderate COVID-19 in patients at high risk for severe disease or hospitalization.

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The ordering process for monoclonal therapy for COVID-19 in outpatients remains the same as outlined below.

Additionally, the criteria for use of casirivimab/imdesivimab have been revised to reflect the FDA's latest EUA guidance:

Patients must be at least 12 years of age, weigh at least 40 kg and have a documented positive result of a direct SARS CoV-2 viral test within the last 10 days AND meet the following clinical criteria listed below:

1) Patient is ≥ 65 years of age
   OR

Patients (ages 12 to 64) with ANY of the following co-morbidities:

2) Obesity or overweight (BMI > 25 kg/m^2 or age 12-17 or have BMI ≥ 85th percentile for their age & gender based on CDC growth charts)
3) Diabetes mellitus
4) Cardiovascular disease (including hypertension or congenital heart disease)
5) Chronic lung disease (e.g., COPD, moderate to severe asthma, interstitial lung disease, cystic fibrosis, pulmonary hypertension)
6) Chronic kidney disease
7) Immunosuppressive disease or immunosuppressive treatment
8) Pregnancy
9) Cirrhosis
10) Parkinson's disease
11) Sickle cell disease
12) Neurodevelopmental disorders (e.g., cerebral palsy) or other conditions that confer medical complexity (e.g., genetic or metabolic syndromes and congenital abnormalities)
13) Having medical-related technology dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID-10])

Exclusion Criteria:

Casirivimab/imdesivimab is not authorized for use in the following patients per the current EUA:

1) Hospitalized due to COVID-19.
   Monoclonal antibodies, such as casirivimab/imdesivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.
   OR
2) Patients who require oxygen therapy due to COVID-19 or who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Referring Patients for Casirivimab/Imdesivimab:

To initiate evaluation of an outpatient for possible monoclonal antibody therapy, enter an ambulatory referral in EPIC for "COVID Antibody Infusion Therapy".

If you do not have access to initiate the referral via EPIC, please use the attached referral form which can be faxed to 475-246-9923.

The above documents are located on the YNHHS COVID-19 Resources for Medical Staff under the "Outpatient Clinical Resources—Medications" which is located at:
https://www.ynhhs.org/patient-care/covid-19/for-employees/for-employees.aspx

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References:

1. Anonymous. Pause in the Distribution of bamlanivimab/etesevimab. June 25, 2021. Available at: https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab-etesevimab/Pages/bamlanivimab-etesevimab-distribution-pause.aspx
2. Anonymous. Full Emergency Use Authorization (EUA) Prescribing Information for Bamlanivimab/Etesevimab. Revised May 14, 2021. Available at: https://www.fda.gov/media/145802/download
3. Anonymous. Full Emergency Use Authorization (EUA) Prescribing Information for Casirivimab/Imdesivimab. Revised June 2021. Available at: https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf
4. COVID Tracker. Connecticut SARS CoV-2 Variant Surveillance. June 24, 2021. Available at: https://covidtrackerct.com/variant-surveillance/