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TO: **YNHHS MEDICAL STAFF**

FROM: **YNHHS COVID-19 TREATMENT TEAM**
YNHHS ANTIMICROBIAL STEWARDSHIP COMMITTEE

SUBJECT: **Criteria for Bamlanivimab & Casirivimab/Imdevimab Use in the Outpatient Setting for the Treatment of COVID-19**

DATE: **December 4, 2020**

Situation:
On November 9, 2020 and then on November 21 ,2020, The US Food and Drug Administration (FDA) granted Emergency Use Authorization (EUA) for bamlanivimab and casirivimab/imdesivimab which are monoclonal antibodies to treat mild to moderate COVID-19 in outpatients.

Background:
Bamlanivimab is a potent anti-spike neutralizing monoclonal antibody that binds with high affinity to the receptor-binding domain of SARS-CoV-2. The BLAZE-1 trial compared bamlanivimab to placebo in outpatients with mild to moderate COVID-19 infection. Bamlanivimab's main clinical endpoint was the percentage of patients who were hospitalized by day 29 of follow-up. The rate of hospitalization for patients who received bamlanivimab was 1.6% (5/309) compared to 6.3% (9/143) who received placebo.

Likewise, casirivimab/imdesivimab are monoclonal antibodies that work in a similar fashion to neutralize the spike protein of COVID-19. R10933-10987-COV-2067 was a randomized, double-blinded, placebo-controlled clinical trial studying casirivimab and imdevimab for the treatment of adult outpatients with mild to moderate COVID-19. Casirivimab/imdevimab's main clinical endpoint was the percentage of patients who were hospitalized by day 29 of follow-up. The rate of hospitalization for patients who received casirivimab/imdevimab was 2% (8/434) compared to 4% (10/231) who received placebo.

Assessment:
Based the above information, the YNHHS COVID-19 Treatment Team and YNHHS Antimicrobial Stewardship Committee met to review the FDA EUA criteria for bamlanivimab and casirivimab/imdevimab.

Given the limited availability of the medication where up to 300,000 doses may only be available to the entire US, there is a need to define which patient populations are at the highest risk for mortality in order to allocate a limited supply of the drug methodically.

In order to define mortality risk from COVID-19 at the population level which included outpatients who tested positive, the above groups reviewed the QCOVID model which was recently published. Based on this data, specific criteria have been developed for eligibility for bamlanivimab and casirivimab/imdevimab.

Note that the current YNHHS criteria are more restrictive than the criteria listed in the FDA's EUA due to the limited supply of these agents.

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Recommendations:

The following are the current YNHHS criteria for bamlanivimab and casirivimab/imdesivimab

Patient must 12 years of age and older and weighing at least 40kg and have a documented positive result of a direct SARS CoV-2 viral test within the last 7 days
AND
who meet the following clinical criteria listed below:

Patients at the highest mortality risk and the number of bamlanivimab doses are severely limited:

a) Patients ≥ 75 years of age
b) Patient less than 75 years of age AND have one of the following co-morbidities:
    1) Chronic Kidney Disease, Stage III or higher or receiving dialysis
    2) Congestive Heart Failure NYHA Class III or higher
    3) Severe pulmonary disease defined as one of the following:
        a) COPD with continuous home oxygen
        b) Pulmonary hypertension or pulmonary fibrosis
        c) Cystic fibrosis
    4) One of the following hematologic/oncologic diagnoses:
        a) S/P stem cell transplant
        b) Active chemotherapy for acute leukemia, lymphoma, or myeloma
    5) S/P solid organ transplant
    6) Immunosuppressive therapy defined as:
        a) Receiving or have received lymphocyte depleting monoclonal antibody therapy (e.g., rituximab, ofatutumab, ocrelizumab, alemtuzumab, etc.)
    7) Parkinson's disease
    8) Patient aged 12-17 with one of the following:
        a) Congenital or acquired heart disease
        b) Neurodevelopmental disorders
        c) Medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19)
        d) Chronic respiratory disease excluding asthma

Exclusion Criteria:
Bamlanivimab and casirivimab/imdesivimab are not authorized for use in patients:

1) Hospitalized due to COVID-19
   Monoclonal antibodies, such as bamlanivimab or 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.

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To order an outpatient referral for an infusion of bamlanivimab or casivirimab/imedevimab, please review the information below:

1) Yale-New Haven Hospital:
   YNHH will initiate outpatient infusions of bamlanivimab or casirivimab/imdevimab starting December 7, 2020. The infusion will administered at the Smilow Rapid Evaluation Clinic on NP-1.

   To initiate evaluation of an outpatient for possible casirivimab/imdevimab, enter an ambulatory referral in EPIC for "COVID Antibody Infusion Therapy".

   For more information on the "COVID Antibody Infusion Therapy" outpatient referral, please review the accompanied "Tips & Tricks" document.

   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.

2) Greenwich Hospital, Bridgeport Hospital, Lawrence + Memorial Hospital, and Westerly Hospital:
   The ad-hoc COVID-19 Antibody Infusion Therapy planning group is working with each hospital to identify sites for infusion and more information will be forthcoming as each site is up and running.

References:

1. Anonymous. Full Emergency Use Authorization (EUA) Prescribing Information for Bamlanivimab. Available at: http://pi.lilly.com/eua/bamlanivimab-eua-factsheet-hcp.pdf.
2. Anonymous. Full Emergency Use Authorization (EUA) Prescribing Information for Available at: https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf
3. Chen P et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. N Engl J Med. 2020 Oct 28. doi: 10.1056/NEJMoa2029849.
4. Clift AK et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. *BMJ* 2020; 371 doi: https://doi.org/10.1136/bmj.m3731
5. Tartof SY, Qian L, Hong V. Obesity and mortality among patients diagnosed with COVID-19: results from an integrated health care organization. *Ann Intern Med*. Published online August 12, 2020. doi:10.7326/M20-3742.