April 21, 2021

Bamlanivimab (Monotherapy)
REVOCATION of Emergency Use Authorization

On April 16, 2021, the U.S. Food and Drug Administration revoked the Emergency Use Authorization (EUA) for bamlanivimab 700mg monotherapy in treating mild-to-moderate COVID-19 in adults and certain pediatric patients (i.e., 12 years of age and older weighing at 40 kg). The FDA's revocation of bamlanivimab removes authorized use only when used alone and does not affect use of the authorized combination product, bamlanivimab and etesevimab. The FDA originally granted the EUA for bamlanivimab monotherapy in November 2020. **Importantly, the EUAs for the monoclonal antibody combinations, including the bamlanivimab plus etesevimab and casirivimab plus imdevimab products, remain in place and continue to be recommended for use as outlined in their respective EUA documents.**

Information provided in the FDA's Letter of Revocation details that following authorization of bamlanivimab for emergency use, there has been a sustained increase in SARS-CoV-2 viral variants across the U.S. that are resistant to bamlanivimab monotherapy. Furthermore, as a function of the FDA's ongoing review of the circumstances and appropriateness of the bamlanivimab monotherapy EUA, the FDA reviewed emerging information and assessed whether, based on the totality of scientific evidence available, the criteria for issuance of the EUA continue to be met. A summary of these new data and new information includes the following[1]:

- *Vesicular stomatitis virus-based pseudovirus expressing spike protein with variant substitutions (in vitro) exhibit large reductions in susceptibility to bamlanivimab alone in neutralization assays.*
- *The Center for Disease Control (CDC) national genomic surveillance program has reported an increasing frequency of SARS-CoV-2 variants that are expected to be resistant to bamlanivimab alone.*
  - *As of mid-March 2021, approximately 20% of isolates sequenced in the U.S. were reported as lineages expected to be resistant to bamlanivimab alone, increasing from approximately 5% in mid-January 2021.*
  - *The CDC national genomic surveillance program has published detailed data regarding variants of the B.1.427 and B.1.429 lineages, first detected in California, which harbor the L452R substitution. These variants have now been identified at frequencies exceeding 20% in eight states and frequencies exceeding 10% in two additional states.*
  - *There are recent reports that variants with the E484K substitution are circulating at rates exceeding 10% in the New York City metropolitan area including northern New Jersey.*
- *Testing technologies that enable health care providers to test individual patients for SARS-CoV-2 viral variants prior to initiation of treatment with monoclonal antibodies are not available and frequencies are changing rapidly. Therefore, empiric treatment with monoclonal antibody therapies that are expected to retain activity broadly across the U.S. is needed to reduce the likelihood of treatment failure.*
- *On April 8, 2021, the National Institutes of Health updated its treatment guidelines for COVID-19 recommending against the use of bamlanivimab alone*.

More information from the FDA, in the form of a Frequently Asked Questions document, can be found here. It is strongly suggested that clinicians review this document as it answers the following questions:

- Why was the EUA for bamlanivimab administered alone (EUA 90) revoked?
- Was the EUA for bamlanivimab alone revoked due to a safety issue?
- Can health care facilities use their current supplies of bamlanivimab?
- If a health care facility has excess supply of bamlanivimab alone, what should the facility do with excess supply?
- Why did FDA issue the EUA for bamlanivimab alone for the treatment of COVID-19 initially?
- Should patients be concerned if they were given bamlanivimab alone to treat COVID-19?
- Is FDA monitoring the SARS-CoV-2 viral variants and their potential impact on other authorized monoclonal antibody treatments?
- Why is the FDA not revoking other monoclonal antibody treatment emergency use authorizations?

References:
1. U.S. Food and Drug Administration. Letter of Revocation. Emergency Use Authorization (EUA) of bamlanivimab. Assessed April 21, 2021.
2. U.S. Food and Drug Administration. Frequently Asked Questions on the Revocation of the Emergency Use Authorization for Bamlanivimab Administered Alone (EUA 90). Assessed April 21, 2021.