U.S. FOOD & DRUG ADMINISTRATION

Frequently Asked Questions on the Emergency Use Authorization of Sotrovimab

Q. What is an Emergency Use Authorization (EUA)?
A: Under section 564 of the Federal Food, Drug & Cosmetic Act, the FDA may, pursuant to a declaration by the HHS Secretary based on one of four types of determinations, authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an EUA, the FDA must determine, among other things, that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; that the known and potential benefits, when used to treat, diagnose or prevent such disease or condition, outweigh the known and potential risks for the product; and that there are no adequate, approved, and available alternatives. Emergency use authorization is NOT the same as FDA approval or licensure.

Q. What does this EUA authorize?
A. This EUA authorizes Sotrovimab, manufactured by GlaxoSmithKline LLC, for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

Q: What does direct SARS-CoV-2 viral testing mean?
A: Direct SARS-CoV-2 viral tests diagnose active COVID-19 infection. Direct SARS-CoV-2 viral tests include two types of diagnostic tests for COVID-19:

- Molecular tests, such as reverse transcription polymerase chain reaction (RT-PCR) tests, that detect the virus's genetic material.
- Antigen tests that detect specific proteins from the virus.

Antibody tests should not be used to diagnose COVID-19 and are not direct SARS-CoV-2 viral tests. Antibody tests look for antibodies that the immune system makes in response to the SARS-CoV-2 virus.

Q. How is high risk defined under the EUA?
A. The following medical conditions or other factors may place adults and pediatric patients (age 12-17 years and weighing at least 40 kg) at higher risk for progression to severe COVID-19:

- Older age (for example age ≥65 years of age)
- Obesity or being overweight (for example, adults with BMI >25 kg/m^2, or if age 12-17, have BMI ≥85th percentile for their age and gender based on CDC growth charts
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- Sickle cell disease

- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
- Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID-19])

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and authorization of sotrovimab under the EUA is not limited to the medical conditions or factors listed above. For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC website: People with Certain Medical Conditions. Healthcare providers should consider the benefit-risk for an individual patient.

Q. Are there limitations of the authorized use under this EUA?

A. Yes. Sotrovimab is not authorized for use in patients:

- who are hospitalized due to COVID-19, or
- 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).

Q. Is sotrovimab a monoclonal antibody? What are monoclonal antibodies?

A. Yes, sotrovimab is a monoclonal antibody. Monoclonal antibodies are laboratory-produced molecules engineered to serve as substitute antibodies that can restore, enhance or mimic the immune system's attack on pathogens. Sotrovimab is designed to block viral attachment and entry into human cells, thus neutralizing the virus.

Q. Does the EUA permit the use of sotrovimab as authorized in patients hospitalized *for reasons other* than COVID-19?

A: Sotrovimab is authorized for emergency use for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

If a patient is hospitalized *for reasons other* than COVID-19, such as for an elective orthopedic procedure, and the patient reports mild to moderate symptoms of COVID-19, confirmed with positive results of a direct SARS-CoV-2 viral test, then it may be appropriate for treatment with sotrovimab if the patient is also at high risk for progression to severe COVID-19, including hospitalization or death, and the terms and conditions of the authorization are met, as detailed in the Fact Sheet for Health Care Providers.

Sotrovimab is not authorized for use in patients:

- who are hospitalized *due to* COVID-19, or
- 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).

Q. When should sotrovimab be administered to a patient?
A. The EUA authorizes sotrovimab to be administered by a qualified healthcare provider as a single intravenous infusion as soon as possible after positive viral test for COVID-19 and within 10 days of symptom onset. More information about administration is available in the Fact Sheet for Health Care Providers.

Q. Where are infusions of sotrovimab available?
A. If you are interested in obtaining sotrovimab under the EUA for the treatment of mild-to-moderate COVID-19 as authorized, please speak with your healthcare provider or contact the GlaxoSmithKline COVID Contact Center at 1-866-GSK-COVID (866-475-2684). More information is available in the Fact Sheet for Patients, Parents, and Caregivers.

Q. Is sotrovimab approved by the FDA to treat COVID-19?
A. No. Sotrovimab is an investigational drug. It is not currently FDA-approved to treat any diseases or conditions, including COVID-19.

Q. Are there data showing sotrovimab might benefit patients with COVID-19?
A. The data supporting benefit for sotrovimab are based on an interim analysis of an ongoing, randomized, double-blind, placebo-controlled clinical trial in 583 non-hospitalized adults with mild-to-moderate COVID-19 symptoms at increased risk for COVID-19 disease progression due to age or other medical conditions. Of these patients, 291 were treated with a single 500-mg infusion of sotrovimab, and 292 received a placebo. Eligible subjects were 18 years of age and older with at least one of the following comorbidities: diabetes, obesity (BMI >30), chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, or moderate to severe asthma, or were 55 years of age and older regardless of comorbidities.

The primary endpoint, progression of COVID-19 at Day 29 (defined as hospitalization for greater than 24 hours for acute management of any illness or death from any cause) was reduced by 85% (adjusted relative risk reduction) in recipients of sotrovimab versus placebo ($p = 0.002$).

Q. Are there clinical trials underway evaluating sotrovimab for COVID-19?
A. Yes. Clinical trials remain ongoing to study sotrovimab for the treatment of COVID-19.

Q. Are there side effects (adverse events) of sotrovimab?
A. Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of sotrovimab in clinical trials. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions have been observed with administration of sotrovimab.

Signs and symptoms of infusion-related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, or dizziness.

There have been reports of clinical worsening of COVID-19 after administration of COVID-19 monoclonal antibodies under EUA; signs or symptoms may include fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, sinus tachycardia, bradycardia), fatigue, and altered mental status. Some of these events required hospitalization. It is not known if these events were related to COVID-19 monoclonal antibody use or were due to progression of COVID-19.

These are not all the possible side effects of sotrovimab. Serious and unexpected side effects may happen. Sotrovimab is still being studied so it is possible that all of the risks are not known at this time.

Q. How can sotrovimab be obtained for use under the EUA?
A. For questions regarding distribution and availability of sotrovimab, please refer to GlaxoSmithKline's webpage.

Q. Are there reporting requirements for healthcare facilities and providers as part of the EUA?
A. Yes. As part of the EUA, FDA requires health care providers who prescribe sotrovimab to report all medication errors and serious adverse events considered to be potentially related to sotrovimab through FDA's MedWatch Adverse Event Reporting program. Providers can complete and submit the report online; or download and complete the form, then submit it via fax at 1-800-FDA-0178. This requirement is outlined in the EUA's Fact Sheet for Health Care Providers. FDA MedWatch forms should also be provided to GlaxoSmithKline.

Q. Do patient outcomes need to be reported under the EUA?
A. No, reporting of patient outcomes is not required under the EUA. However, reporting of all medication errors and serious adverse events considered to be potentially related to sotrovimab is required.

Q. Does the EUA authorize sotrovimab to be used to prevent COVID-19?
A. No. Sotrovimab is not authorized for the prevention of COVID-19.

Q. Can health care providers share the Fact Sheet for Patient, Parents, and Caregivers electronically?
A. The letter of authorization for sotrovimab permits GlaxoSmithKline and its authorized distributors make the Fact Sheets available to healthcare facilities and health care providers through electronic means.

Q. Can I be vaccinated for COVID-19 if I was treated with a monoclonal antibody for COVID-19?
A. Currently, there are no data on the safety and effectiveness of the Pfizer-BioNTech, Moderna, or Janssen COVID-19 vaccine in people who received monoclonal antibodies authorized by FDA for emergency use as part of COVID-19 treatment (sotrovimab, casirivimab and imdevimab, or bamlanivimab and etesevimab). The Advisory Committee on Immunization Practices (ACIP) currently recommends COVID-19 vaccination be deferred for at least 90 days after treatment with a monoclonal antibody for COVID-19. Updates to this recommendation may be made as additional information on the interaction between prior monoclonal antibody treatment and vaccine response becomes available.

Q. How are the monoclonal antibody therapies affected by the SAR-CoV-2 viral variants in the U.S.?
A: Circulating SARS-CoV-2 viral variants may be associated with resistance to monoclonal antibodies. The frequency of these variants is being monitored by the FDA, Centers for Disease Control and Prevention (CDC), and other stakeholders. Health care providers should review the Antiviral Resistance information in Section 15 of the authorized Fact Sheets for each monoclonal antibody therapy available under an EUA for details regarding specific variants and resistance. Health care providers should also refer to the CDC website on Variant Proportions, and information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.