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, based on the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe 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? Are there limitations of the authorized use under this EUA?

A. This EUA authorizes sotrovimab, manufactured by GlaxoSmithKline LLC, to be used only 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.

Limitations of Authorized Use

Sotrovimab is not authorized for use in:

- Adults and pediatric patients who are hospitalized due to COVID-19, or
- Adult and pediatric patients who require oxygen therapy and/or respiratory support due to COVID-19, or
- Adult and pediatric patients who require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 in those patients on chronic oxygen.

Benefit of treatment with sotrovimab has **not** been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as sotrovimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Sotrovimab is not authorized for treatment of mild-to-moderate COVID-19 in geographic regions where infection is likely to have been caused by a non-susceptible SARSCoV-2 variant based on available information including variant susceptibility to these drugs and regional variant frequency.

- FDA will monitor conditions to determine whether use in a geographic region is consistent with this scope of authorization, referring to available information, including information on variant susceptibility [see Microbiology/Resistance Information (15) in the Fact Sheet for Health Care Providers], and CDC's regional variant frequency data.
- FDA's determination and any updates will be available at Emergency Use Authorizations for Drugs and Non-Vaccine Biological Products.

For other limitations and conditions, refer to the EUA.

Q. How are the monoclonal antibody therapies affected by the SARS-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.

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. Can adults weighing less than 40 kg receive sotrovimab?
A. Yes. Sotrovimab is authorized 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. Adults can be treated regardless of their weight; pediatric patients must be at least 12 years of age and weigh at least 40 kg.

Q. When should sotrovimab be administered to a patient?
A. Sotrovimab should be administered by a qualified healthcare provider as a single intravenous infusion (IV) as soon as possible after positive viral test for COVID-19 **and** within seven (7) days of symptom onset. More information about administration is available in the Fact Sheet for Health Care Providers.

Q. Does "within seven (7) days of symptom onset" mean that a patient should have shown symptoms to receive sotrovimab for treatment of COVID-19?
A. Yes. Symptom onset is the point at which a patient starts exhibiting symptoms. Patients should be treated as soon as possible after a positive viral test for SARS-CoV-2 **and** within seven (7) days of COVID-19 symptom onset. If a patient has a positive viral test for SARS-CoV-2 but does not show symptoms, they do not meet the definition of mild-to-moderate disease. Patients with mild-to-moderate COVID-19 are those patients who are actively exhibiting certain symptoms of COVID-19 illness (such as, fever, cough, sore throat, headache, malaise, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell).

Therefore, patients with mild-to-moderate COVID-19 disease (i.e., symptoms consistent with mild-to-moderate illness at the time of treatment) who are at high risk for progression to severe COVID-19, including hospitalization or death, and who have positive results of direct SARS-CoV-2 viral testing and who are within seven (7) days of symptom onset are within the scope of the EUA.

For more information on mild-to-moderate COVID-19, refer to the National Institutes of Health's website at: Clinical Spectrum of COVID-19 Treatment Guidelines (nih.gov).

Q. Does the EUA permit the use of sotrovimab as authorized in patients hospitalized *for reasons other* than COVID-19?
A. Yes. 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 treatment with sotrovimab may be appropriate, 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:

- Adults and pediatric patients who are hospitalized due to COVID-19, or
- Adult and pediatric patients who require oxygen therapy and/or respiratory support due to COVID-19, or
- Adult and pediatric patients who require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 in those patients on chronic oxygen.

Q. How can sotrovimab be obtained for use under the EUA?
A. For questions on how to obtain sotrovimab under current distribution procedures, please contact COVID19therapeutics@hhs.gov.

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. 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 entry into human cells, thus neutralizing the virus.

Q. Are there data showing sotrovimab might benefit patients with COVID-19?
A. The initial data supporting benefit for sotrovimab are based on an analysis of an ongoing, randomized, double-blind, placebo-controlled clinical trial in 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 the 1,057 patients enrolled, 528 were treated with a single 500-mg infusion of sotrovimab, and 529 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 79% (adjusted relative risk reduction) in recipients of sotrovimab versus placebo (95% confidence interval [50%, 91%]).

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 on how to obtain sotrovimab under current distribution procedures, please contact COVID19therapeutics@hhs.gov.

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. Health care providers should refer to recommendations of the Advisory Committee on Immunization Practices regarding vaccination.