



June 8, 2021

Sotrovimab (monoclonal antibody)

- EMERGENCY USE AUTHORIZATION -

Mechanism of action¹: Sotrovimab is a recombinant human IgG1κ monoclonal antibody that binds to a conserved epitope on the spike protein receptor binding domain of SARS-CoV-2. Sotrovimab does not compete with human ACE2 receptor binding.

Current Status^{1,2}: Sotrovimab is not FDA-approved. On May 16, 2021, the U.S. Food and Drug Administration issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product sotrovimab for the treatment of mild-to-moderate coronavirus disease 2019 (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, to treat 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.

The following medical conditions or other factors may place adults and pediatric patients (12 to 17 years of age weighing at least 40 kg) at higher risk for progression to severe COVID-19:

- Older age (for example ≥ 65 years of age)
- Obesity or being overweight (for example, adults with BMI > 25 kg/m², or if 12 to 17 years of age, have BMI ≥ 85 th percentile for their age and gender based on [CDC growth charts](#),
- Pregnancy
- Chronic kidney disease or Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (COPD, asthma, interstitial lung disease, cystic fibrosis and pulmonary HTN)
- 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 (e.g., 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. Healthcare providers should consider the benefit-risk for individual patients.

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).

*****Benefit of treatment with sotrovimab has not been observed in patients hospitalized due to COVID-19. SARS-CoV-2 monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.***

Availability: Unlike other EUA medications, the US Government will not be directly providing this product to the IHS. If you are interested in obtaining sotrovimab under the EUA for the treatment of mild-to-moderate COVID-19, please contact the IHS National Supply Service Center, c/o CDR Miller (matthew.miller@ihs.gov).

Dosing and Administration²: The dosage of sotrovimab is 500 mg and it must be administered after dilution by intravenous (IV) infusion only. Sotrovimab should be given as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset. Sotrovimab must be diluted and administered as a single intravenous infusion over 30 minutes. Furthermore, sotrovimab may only be administered in settings in which healthcare providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary. No dosage adjustment is recommended based on renal impairment, during pregnancy or while lactating

Efficacy²⁻⁴: Data supporting the sotrovimab EUA are based on an interim analysis from a phase 1/2/3 randomized, double-blind, placebo-controlled clinical trial (COMET-ICE trial, [NCT #04545060](#)) in 583 non-hospitalized adults with mild-to-moderate COVID-19 symptoms and a positive SARS-CoV-2 test result. Of these patients, 291 received sotrovimab and 292 received a placebo within 5 days of onset of COVID-19 symptoms. The primary endpoint was progression of COVID-19 (defined as hospitalization for ≥ 24 hours for acute management of any illness or death from any cause) through day 29. Hospitalization or death occurred in 21 (7%) patients given placebo vs. 3 (1%) patients treated with sotrovimab, an 85% risk reduction ($p=0.002$).

There is a potential risk of treatment failure due to the development of viral variants that are resistant to sotrovimab. Prescribing healthcare providers should consider the prevalence of SARS-CoV-2 variants in their area, where data are available, when considering treatment options. Health care providers can 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.

Safety / Adverse Drug Events²: The safety of sotrovimab is primarily based on an interim analysis from 868 patients through Day 15 in the COMET-ICE trial. Reported events that started within 24 hours of study treatment were pyrexia, chills, dizziness, dyspnea, pruritus, rash, and infusion-related reactions; all events were Grade 1 (mild) or Grade 2 (moderate). The most common treatment-emergent adverse events observed in the sotrovimab treatment group in COMET-ICE were rash (2%) and diarrhea (1%), all of which were Grade 1 (mild) or Grade 2 (moderate). No other treatment-emergent adverse events were reported at a higher rate with sotrovimab compared to placebo.

Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of sotrovimab. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Mandatory Requirements under the EUA¹⁻³:

1. Use sotrovimab only in authorized patient populations as described above.
2. Communicate to patients or parents/caregivers, as age appropriate, information consistent with the [“Fact Sheet for Patients, Parents and Caregivers”](#) prior to patients receiving sotrovimab. **Healthcare providers** (to the extent practicable given the circumstances of the emergency) **must document in the patient’s medical record that the patient/caregiver has been:**
 - Given the “Fact Sheet for Patients, Parents and Caregivers”,
 - Informed of alternatives to receiving authorized sotrovimab, and
 - Informed that sotrovimab is an unapproved drug authorized for use under this EUA.
3. Avoid use in patients with known hypersensitivity to any ingredient of sotrovimab.
4. The prescriber is responsible for mandatory reporting of all drug errors and serious adverse events to FDA Medwatch within 7 calendar days from onset of the event.
 - Reports should include the words “use of sotrovimab was under EUA” in the “Describe Event” section.
 - Reports should include the words “Indian Health Service” or “IHS” on the form in the reporter section (section G)
 - Information on the FDA MedWatch program can be found on the [IHS Pharmacovigilance website](#).

References:

1. U.S. Food and Drug Administration. [Letter of Authorization](#). Emergency Use Authorization (EUA) of sotrovimab.
2. U.S. Food and Drug Administration. [Fact Sheet for Health Care Providers](#). Emergency Use Authorization (EUA) of sotrovimab.
3. U.S. Food and Drug Administration. FDA News Release, May 26, 2021. [Coronavirus \(COVID-19\) Update: FDA Authorizes Additional Monoclonal Antibody for Treatment of COVID-19](#). Accessed June 2, 2021.
4. U.S. Food and Drug Administration. [Frequently Asked Questions on the Emergency Use Authorization of Sotrovimab](#). Accessed June 2, 2021.