

**SOTROVIMAB- sotrovimab injection, solution, concentrate**  
**GlaxoSmithKline LLC**

*Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.*

**FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR SOTROVIMAB**

**HIGHLIGHTS OF EMERGENCY USE AUTHORIZATION (EUA)**

**These highlights of the EUA do not include all the information needed to use SOTROVIMAB under the EUA. See the FULL FACT SHEET FOR HEALTHCARE PROVIDERS for SOTROVIMAB.**

**SOTROVIMAB injection, for intravenous use**  
**Original EUA Authorized Date: 05/2021**

**RECENT MAJOR CHANGES**

-  
Clinical Pharmacology, Microbiology (12.4) 3/2023  
Emergency Use Authorization, Limitations of Authorized Use (1) 2/2022  
Dosage and Administration, Recommended Dosage (2.3) 2/2022  
Dosage and Administration, Preparation and Administration (2.5) 2/2022

**EUA FOR SOTROVIMAB**

- The Secretary of Health and Human Services has issued an EUA for the emergency use of sotrovimab for the treatment of mild-to-moderate

**WARNINGS AND PRECAUTIONS**

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions: Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of sotrovimab. If clinically significant hypersensitivity reactions or anaphylaxis occur, discontinue and initiate appropriate supportive care. Infusion-related reactions have occurred during the infusion and up to 24 hours post infusion. These reactions may be severe or life threatening. (5.1)  
Clinical Worsening After SARS-CoV-2 Monoclonal Antibody Administration: Clinical worsening of COVID-19 after administration of SARS-CoV-2 monoclonal antibody treatment has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, tachycardia, bradycardia), fatigue, and altered mental status. (5.2)  
Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19: 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.

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.

However, sotrovimab is not approved for this use (i.e., sotrovimab has not been demonstrated to be safe and effective for this use).

Limitations of Use:

- Sotrovimab is not authorized for treatment of mild-to-moderate COVID-19 when infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant based on available information including variant susceptibility to these drugs and regional variant frequency(1, 12.4).
  - o FDA’s determination and any updates will be available at: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs>.
- Sotrovimab is not authorized for use in patients who:
  - o are hospitalized due to COVID-19, OR
  - o require oxygen therapy and/or respiratory support due to COVID-19, OR
  - o require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 in those patients on chronic oxygen.

See Full Fact Sheet for Healthcare Providers for the justification for emergency use of drugs during the

(5.3)

----- **ADVERSE REACTIONS** -----

The most common adverse reactions (incidence  $\geq 1\%$ ) included rash, diarrhea, infusion-related reactions, and hypersensitivity adverse reactions. (6.1)

**You or your designee must report all SERIOUS ADVERSE EVENTS or MEDICATION ERRORS potentially related to sotrovimab (1) by submitting FDA Form 3500 online, (2) by downloading this form and then submitting by mail or fax, or (3) contacting the FDA at 1-800-FDA-1088 to request this form. Please also provide a copy of this form to GSK, Global Safety: Fax: 919-287-2902; E-mail: [WW.GSKAEReportingUS@gsk.com](mailto:WW.GSKAEReportingUS@gsk.com); or call GSK at 1-866-475-2684 to report adverse events. (6.4)**

----- **DRUG INTERACTIONS** -----

Clinical drug-drug interaction studies have not been performed with sotrovimab. Sotrovimab is not renally excreted or metabolized by cytochrome P450 (CYP) enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of CYP enzymes are unlikely. (7)

**See PATIENT AND PARENTS/CAREGIVER FACT SHEET.**

COVID-19 pandemic, information on available alternatives, and additional information on COVID-19 (1).

----- **DOSAGE AND ADMINISTRATION** -----

--

- The recommended dosage of sotrovimab in patients 12 years of age and older weighing at least 40 kg is 500 mg administered as a single intravenous infusion. (2.2)
- See Full Prescribing Information for instructions on preparation and administration. (2.4)

----- **DOSAGE FORMS AND STRENGTHS** -----

Injection: 500 mg/8 mL (62.5 mg/mL) single-dose vial. (3)

----- **CONTRAINDICATIONS** -----

History of anaphylaxis to sotrovimab or to any of the excipients in the formulation. (4)

---

**TABLE OF CONTENTS\***

**1 EMERGENCY USE AUTHORIZATION**

**2 DOSAGE AND ADMINISTRATION**

2.1 Patient Selection

2.2 Important Administration Information

2.3 Recommended Dosage

2.4 Dosage Adjustment in Special Populations

2.5 Preparation and Administration

**3 DOSAGE FORMS AND STRENGTHS**

**4 CONTRAINDICATIONS**

**5 WARNINGS AND PRECAUTIONS**

5.1 Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

5.2 Clinical Worsening after SARS-CoV-2

**8 USE IN SPECIFIC POPULATIONS**

8.1 Pregnancy

8.2 Lactation

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Renal Impairment

8.7 Hepatic Impairment

**10 OVERDOSAGE**

**11 DESCRIPTION**

**12 CLINICAL PHARMACOLOGY**

12.1 Mechanism of Action

12.3 Pharmacokinetics

12.4 Microbiology

Monoclonal Antibody Administration  
5.3 Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

## **6 ADVERSE REACTIONS**

6.1 Adverse Reactions from Clinical Studies

6.2 Adverse Reactions from Spontaneous Reports

6.4 Required Reporting for Serious Adverse Events and Medication Errors

## **7 DRUG INTERACTIONS**

12.6 Immunogenicity

## **13 NONCLINICAL TOXICOLOGY**

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

13.2 Animal Toxicology and/or Pharmacology

## **14 CLINICAL STUDIES**

## **16 HOW SUPPLIED/STORAGE AND HANDLING**

## **17 PATIENT COUNSELING INFORMATION**

## **18 MANUFACTURER INFORMATION**

\* Sections or subsections omitted from the EUA are not listed

---

## **FULL FACT SHEET FOR HEALTHCARE PROVIDERS**

### **1 EMERGENCY USE AUTHORIZATION**

The Secretary of Health and Human Services (HHS) has issued an Emergency Use Authorization (EUA) for the emergency use of 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. However, sotrovimab is not approved for this use (i.e., sotrovimab has not been demonstrated to be safe and effective for this use).

### **LIMITATIONS OF AUTHORIZED USE**

- Sotrovimab is not authorized for treatment of mild-to-moderate COVID-19 when infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant based on available information including variant susceptibility to these drugs and regional variant frequency [see *Microbiology (12.4)*].
  - o FDA's determination and any updates will be available at: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs>.<sup>1</sup>
- Sotrovimab is not authorized for use in patients who:
  - o are hospitalized due to COVID-19, OR
  - o require oxygen therapy and/or respiratory support due to COVID-19, OR
  - o 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. 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 [see *Warnings and Precautions (5.2)*].

Sotrovimab is not FDA-approved for any use, including for the treatment of COVID-19.

Sotrovimab is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of sotrovimab under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

### Justification for Emergency Use of Drugs During the COVID-19 Pandemic

There is currently an outbreak of Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2, a novel coronavirus. The Secretary of HHS has declared that:

- A public health emergency related to COVID-19 has existed since January 27, 2020.
- Circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic (March 27, 2020 declaration).

An EUA is a Secretary of HHS authorization for the emergency use of an unapproved product or unapproved use of an approved product (i.e., drug, biological product, or device) in the United States under certain circumstances including, but not limited to, when the Secretary of HHS declares that there is a public health emergency that affects the national security or the health and security of United States citizens living abroad, and that involves biological agent(s) or a disease or condition that may be attributable to such agent(s). Criteria for issuing an EUA include:

- The biological agent(s) can cause a serious or life-threatening disease or condition;
- Based on the totality of the available scientific evidence (including data from adequate and well-controlled clinical trials, if available), it is reasonable to believe that
  - o the product may be effective in diagnosing, treating, or preventing the serious or life-threatening disease or condition; and
  - o the known and potential benefits of the product - when used to diagnose, prevent, or treat such disease or condition - outweigh the known and potential risks of the product, taking into consideration the material threat posed by the biological agent(s);
- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the serious or life-threatening disease or condition.

### Information Regarding Available Alternatives for the EUA Authorized Use

Veklury (remdesivir) is FDA-approved for the treatment of COVID-19 in adults and pediatric patients (28 days of age and older and weighing at least 3 kg) who are hospitalized, or who are not hospitalized, have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death. Veklury is administered via intravenous infusion for a total treatment duration of 3 days in patients who are not hospitalized.

Although Veklury is an approved alternative treatment of mild-to-moderate COVID-19 in adults and pediatric patients (28 days of age and older and weighing at least 3 kg) who

are not hospitalized and have mild-to-moderate COVID-19, FDA does not consider Veklury to be an adequate alternative to sotrovimab for this authorized use because it may not be feasible or clinically appropriate for certain patients.

Other therapeutics are currently authorized under Emergency Use Authorization for the same use as sotrovimab. For additional information on all products authorized for treatment or prevention of COVID-19, please see <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>.

For information on clinical studies of sotrovimab and other therapies for the treatment of COVID-19, see [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

---

1 FDA will monitor conditions to determine whether the use of sotrovimab is consistent with this scope of authorization, referring to available information, including information on variant susceptibility [see *Microbiology (12.4)*], and the CDC national and/or regional variant frequency data available at: <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Patient Selection

Sotrovimab is authorized for the use in adults and pediatric patients (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death [see *Clinical Studies (14)*].

Medical conditions or other factors that may place individual patients at higher risk for progression to severe COVID-19 are listed on the following CDC website: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>.

### 2.2 Important Administration Information

Sotrovimab should be administered intravenously within 7 days of symptom onset.

Sotrovimab should be administered by a qualified healthcare professional and administered only in settings which 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 [see *Warnings and Precautions (5.1)*].

Sotrovimab is available as a concentrated solution and **must be diluted** prior to IV infusion.

Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.

### 2.3 Recommended Dosage

The recommended dosage for emergency use of sotrovimab authorized under this EUA is 500 mg administered as a single IV infusion over 15 minutes for 50-mL infusion bag or 30 minutes for 100-mL infusion bag.

### 2.4 Dosage Adjustment in Special Populations

No dosage adjustment is recommended in pregnant or lactating women, in elderly patients, or in patients with renal impairment [*see Use in Specific Populations (8)*].

### Pediatric Use

No dosage adjustment is recommended in pediatric patients who weigh at least 40 kg and are 12 years of age and older.

Sotrovimab is not authorized for patients under 12 years of age or in pediatric patients weighing less than 40 kg [*see Use in Specific Populations (8.4)*].

## **2.5 Preparation and Administration**

### Preparation

Sotrovimab is supplied in a single-dose vial and **must be diluted** prior to IV infusion.

Sotrovimab concentrate for solution for infusion should be prepared by a qualified healthcare professional using aseptic technique.

- Gather a polyvinyl chloride (PVC) or polyolefin (PO), sterile, prefilled 50-mL or 100-mL infusion bag containing 0.9% Sodium Chloride Injection or 5% Dextrose Injection.
- Remove one vial of sotrovimab (500 mg/8 mL) from refrigerated storage and allow to equilibrate to room temperature, protected from light, for approximately 15 minutes.
- Inspect the vial of sotrovimab visually for particulate matter and discoloration prior to administration. Should either be observed, the solution must be discarded, and fresh solution prepared. Sotrovimab is a clear, colorless or yellow to brown solution.
- Gently swirl the vial several times before use without creating air bubbles. **Do not shake the vial.**
- Withdraw 8 mL of sotrovimab from the vial and inject into the prefilled infusion bag.
- Discard vial (even if some product remains).
- Prior to the infusion, gently rock the infusion bag back and forth by hand 3 to 5 times. **Do not invert the infusion bag.** Avoid forming air bubbles.
- This product is preservative-free; therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted solution of sotrovimab up to 6 hours at room temperature (up to 25°C [77°F]) or refrigerated up to 24 hours (2°C to 8°C [36°F to 46°F]).

### Administration

Sotrovimab infusion solution should be administered by a qualified healthcare professional [*see Warnings and Precautions (5.1)*].

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 [*see Warnings and Precautions (5.1)*].

- Gather the materials for IV infusion via infusion pump or gravity:
  - o Polyvinyl chloride (PVC) or polyolefin (PO) infusion set, and

- o Use of a 0.2 micron polyethersulfone (PES) filter is strongly recommended.
- Attach the infusion set to the IV bag using standard bore tubing.
- Prime the infusion set.
- Administer the entire infusion over 15 minutes for 50-mL infusion bag or 30 minutes for 100-mL infusion bag. Due to potential overfill of prefilled saline bags, the entire infusion solution in the bag should be administered to avoid underdosage.
- Do not administer as an IV push or bolus.
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of sotrovimab with IV solutions and medications other than 0.9% Sodium Chloride Injection and 5% Dextrose Injection is not known.
- Once infusion is complete, **flush the tubing** with 0.9% Sodium Chloride or 5% Dextrose to ensure delivery of the required dose.
- If the infusion must be discontinued due to an infusion reaction, discard unused product.
- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.

### **3 DOSAGE FORMS AND STRENGTHS**

Sotrovimab is a sterile, preservative-free, clear, colorless or yellow to brown solution for IV infusion only available as:

- Injection: 500-mg/8-mL (62.5-mg/mL) solution in a single-dose vial

### **4 CONTRAINDICATIONS**

Sotrovimab is contraindicated in patients who have a history of anaphylaxis to sotrovimab or to any of the excipients in the formulation.

### **5 WARNINGS AND PRECAUTIONS**

There are limited clinical data available for sotrovimab. Serious and unexpected adverse events may occur that have not been previously reported with sotrovimab use.

#### **5.1 Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions**

Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of sotrovimab [see *Adverse Reactions (6.1)*]. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions, occurring during the infusion and up to 24 hours after the infusion, have been observed with administration of sotrovimab. These reactions may be severe or life threatening.

Signs and symptoms of infusion-related reactions may include [see *Adverse Reactions (6.1)*]:

- fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia



(e.g., atrial fibrillation, sinus tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, vaso-vagal reactions (e.g., pre-syncope, syncope), dizziness, and diaphoresis.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care. Clinically monitor patients for at least 1 hour after completion of the infusion for signs and symptoms of hypersensitivity.

Hypersensitivity reactions occurring more than 24 hours after the infusion have also been reported with the use of SARS-CoV-2 monoclonal antibodies under Emergency Use Authorization.

## **5.2 Clinical Worsening after SARS-CoV-2 Monoclonal Antibody Administration**

Clinical worsening of COVID-19 after administration of SARS-CoV-2 monoclonal antibody treatment has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, tachycardia, bradycardia), fatigue, and altered mental status. Some of these events required hospitalization. It is not known if these events were related to SARS-CoV-2 monoclonal antibody use or were due to progression of COVID-19.

## **5.3 Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19**

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. Therefore, sotrovimab is not authorized for use in the following patient populations [see *Limitations of Authorized Use (1)*]:

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

## **6 ADVERSE REACTIONS**

The following serious adverse reaction is described in more detail in the *Warnings and Precautions* section of the labeling:

- Hypersensitivity including anaphylaxis and infusion related reactions [see *Warnings and Precautions (5.1)*].

### **6.1 Adverse Reactions from Clinical Studies**

The following adverse reactions have been observed in the clinical studies of sotrovimab that supported EUA. The adverse reaction rates observed in these clinical studies cannot be directly compared to rates in the clinical studies of another drug and may not reflect

the rates observed in clinical practice. Additional adverse events associated with sotrovimab may become apparent with more widespread use.

The safety of sotrovimab in subjects with mild-to-moderate COVID-19 (subjects with COVID-19 symptoms who are not hospitalized) is based on analyses from COMET-ICE and COMET-TAIL [see *Clinical Studies (14)*].

In COMET-ICE, subjects received a single 500-mg IV infusion of sotrovimab (n = 523) or placebo (n = 526). In COMET-TAIL, subjects received a single 500-mg IV infusion of sotrovimab (n = 393).

#### Infusion-Related Reactions Including Hypersensitivity

Infusion-related reactions, including immediate hypersensitivity reactions, were observed in 1% of subjects treated with sotrovimab and 1% of subjects treated with placebo in COMET-ICE and in <1% of subjects treated with IV sotrovimab in COMET-TAIL. 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).

One case of anaphylaxis was reported following sotrovimab infusion in a separate study evaluating sotrovimab in hospitalized subjects; the infusion was immediately discontinued, and the subject received epinephrine. The event resolved but recurred within 2 hours; the subject received another dose of epinephrine and improved with no additional symptoms. Other serious infusion-related reactions (including immediate hypersensitivity reactions) reported following sotrovimab infusion in the hospitalized study included Grade 3 (serious) or Grade 4 (life-threatening) bronchospasm and shortness of breath. These events were also reported following infusion of placebo. Sotrovimab is not authorized for use in subjects hospitalized due to COVID-19 [see *Warnings and Precautions (5.3)*].

Hypersensitivity adverse reactions (i.e., adverse events assessed as causally related) were observed in 2% of subjects treated with sotrovimab and 1% of subjects treated with placebo in COMET-ICE and in <1% of subjects treated with sotrovimab in COMET-TAIL. All were Grade 1 (mild) or Grade 2 (moderate), and none of the reactions in either trial led to permanent discontinuation of the infusions. One reaction led to pausing of the infusion [see *Warnings and Precautions (5.1)*].

#### Common Adverse Events

The most common treatment-emergent adverse events observed in the sotrovimab treatment group in COMET-ICE were rash (1%) and diarrhea (2%), 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.

### **6.2 Adverse Reactions from Spontaneous Reports**

The following adverse reactions have been identified during post-authorization use of sotrovimab. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

#### Immune System Disorders

Anaphylaxis [see *Contraindications (4)*, *Warnings and Precautions (5.1)*].

## 6.4 Required Reporting for Serious Adverse Events and Medication Errors

The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events\* and medication errors potentially related to sotrovimab within 7 calendar days from the healthcare provider's awareness of the event, using FDA Form 3500 (for information on how to access this form, see below). The FDA requires that such reports, using FDA Form 3500, include the following:

- Patient demographics and baseline characteristics (e.g., patient identifier, age or date of birth, gender, weight, ethnicity, and race)
- A statement "Sotrovimab use for COVID-19 under Emergency Use Authorization (EUA)" under the "**Describe Event, Problem, or Product Use/Medication Error**" heading
- Information about the serious adverse event or medication error (e.g., signs and symptoms, test/laboratory data, complications, timing of drug initiation in relation to the occurrence of the event, duration of the event, treatments required to mitigate the event, evidence of event improvement/disappearance after stopping or reducing the dosage, evidence of event reappearance after reintroduction, clinical outcomes)
- Patient's preexisting medical conditions and use of concomitant products
- Information about the product (e.g., dosage, route of administration, NDC #)

Submit adverse event and medication error reports, using Form 3500, to FDA MedWatch using one of the following methods:

- Complete and submit the report online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm), or
- Complete and submit a postage-paid FDA Form 3500 (<https://www.fda.gov/media/76299/download>) and return by:
  - o Mail to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787, or
  - o Fax to 1-800-FDA-0178, or
- Call 1-800-FDA-1088 to request a reporting form.
- In addition, please provide a copy of all FDA MedWatch forms to:  
GlaxoSmithKline, Global Safety  
Fax: 919-287-2902  
Email: [WW.GSKAEReportingUS@gsk.com](mailto:WW.GSKAEReportingUS@gsk.com)  
Or call GSK at 1-866-475-2684 to report adverse events.

The prescribing health care provider and/or the provider's designee is/are responsible for mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of sotrovimab.

\*Serious adverse events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- Other important medical event, which may require a medical or surgical intervention

to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

## **7 DRUG INTERACTIONS**

Clinical drug-drug interaction studies have not been performed with sotrovimab. Sotrovimab is not renally excreted or metabolized by cytochrome P450 (CYP) enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of CYP enzymes are unlikely.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to sotrovimab during pregnancy. Pregnant and recently pregnant individuals can go to <https://covid-pr.pregistry.com> to enroll or call 1-800-616-3791 to obtain information about the registry.

#### Risk Summary

There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcome. Sotrovimab should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus. There are maternal and fetal risks associated with untreated COVID-19 in pregnancy (*see Clinical Considerations*).

Nonclinical reproductive toxicity studies have not been conducted with sotrovimab. In a cross-reactive binding assay using a protein array enriched for human embryofetal proteins, no off-target binding was detected for sotrovimab. Since sotrovimab is a recombinant human immunoglobulin G (IgG) containing the LS modification in the Fc domain, it has the potential for placental transfer from the mother to the developing fetus. The potential treatment benefit or risk of placental transfer of sotrovimab to the developing fetus is not known.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

#### Clinical Considerations

##### *Disease-Associated Maternal and/or Embryo-Fetal Risk*

COVID-19 in pregnancy is associated with adverse maternal and fetal outcomes, including preeclampsia, eclampsia, preterm birth, premature rupture of membranes, venous thromboembolic disease, and fetal death.

### **8.2 Lactation**

## Risk Summary

There are no available data on the presence of sotrovimab in human or animal milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for sotrovimab and any potential adverse effects on the breastfed infant from sotrovimab or from the underlying maternal condition. Individuals with COVID-19 who are breastfeeding should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

### **8.4 Pediatric Use**

Sotrovimab is not authorized for use in pediatric patients under 12 years of age or weighing less than 40 kg. The safety and effectiveness of sotrovimab have not been assessed in pediatric patients. The recommended dosing regimen in patients 12 years to less than 18 years of age, weighing at least 40 kg, is expected to result in comparable serum exposures of sotrovimab as those observed in adults.

### **8.5 Geriatric Use**

Of the 528 subjects randomized to receive sotrovimab 500 mg in COMET-ICE, 20% were 65 years of age and older and 11% were over 70 years of age. Of the 378 subjects in the primary analysis population receiving sotrovimab 500 mg in COMET-TAIL, 25% were 65 years of age or older and 8% were over 75 years of age. In these trials, no notable differences in PK or safety were observed in geriatric subjects as compared to subjects less than 65 years of age.

### **8.6 Renal Impairment**

No clinical trials have been conducted to evaluate the effects of renal impairment on the PK of sotrovimab. Sotrovimab is not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of sotrovimab.

### **8.7 Hepatic Impairment**

No clinical trials have been conducted to evaluate the effects of hepatic impairment on the PK of sotrovimab. The impact of hepatic impairment on the PK of sotrovimab is unknown.

## **10 OVERDOSAGE**

There is no human experience of acute overdosage with sotrovimab.

There is no specific treatment for an overdose with sotrovimab. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

## **11 DESCRIPTION**

Sotrovimab is a human immunoglobulin G-1 (IgG1-kappa) monoclonal antibody consisting of 2 identical light chain (LC) polypeptides composed of 214 amino acids each and 2 identical heavy chain (HC) polypeptides, each composed of 457 amino acids. Sotrovimab is produced by a Chinese Hamster Ovary cell line and has a molecular weight

of approximately 149 kDa.

Sotrovimab injection is a sterile, preservative-free, clear, colorless or yellow to brown solution supplied in a single-dose vial for IV infusion after dilution.

Each mL contains sotrovimab (62.5 mg), L-histidine (1.51 mg), L-histidine monohydrochloride (2.15 mg), L-methionine (0.75 mg), polysorbate 80 (0.4 mg), and sucrose (70 mg). The solution of sotrovimab has a pH of 6.0.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Sotrovimab is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antiviral drug [*see Microbiology (12.4)*].

### 12.3 Pharmacokinetics

A summary of pharmacokinetic parameters following a single 500-mg IV infusion is presented in Table 1 based on population pharmacokinetic analyses:

**Table 1. Summary of IV Sotrovimab Serum Pharmacokinetic Exposure Parameters**

Parameter <sup>a</sup>	Sotrovimab (500 mg IV)
C <sub>max</sub> , mcg/mL	170.1 (53.4)
C <sub>D28</sub> , mcg/mL	39.7 (37.6)
AUC <sub>D0-28</sub> <sup>b</sup> , day*mcg/mL	1564 (34.4)

<sup>a</sup> Parameters are reported as geometric mean (Geometric %CV).

<sup>b</sup> Based on a population pharmacokinetic analysis using data from a total of 1984 subjects across 5 clinical trials.

The primary analysis in the clinical efficacy study COMET-ICE was conducted when the ancestral Wuhan-Hu-1 virus was predominant, with the most common SARS-CoV-2 variants being Alpha and Epsilon among participants in the study population, which was enrolled prior to the emergence of the Delta and Omicron variants (Table 3).

#### Specific Populations

Based on available population pharmacokinetic analyses of sotrovimab dosages of 500 mg or less, the pharmacokinetics of sotrovimab administered intravenously were not affected by age or sex; body weight was identified as a significant covariate on the pharmacokinetics of sotrovimab, but the impact is not anticipated to be clinically relevant.

Renal impairment is not expected to impact the pharmacokinetics of sotrovimab since mAbs with molecular weight >69 kDa do not undergo renal elimination. Similarly, dialysis is not expected to impact the pharmacokinetics of sotrovimab.

### 12.4 Microbiology

#### Mechanism of Action

Sotrovimab is a recombinant human IgG1-kappa mAb that binds to a conserved epitope on the spike protein receptor binding domain of SARS-CoV-2 with a dissociation constant of  $K_D = 0.21$  nM but does not compete with human ACE2 receptor binding ( $IC_{50}$  value  $>33.6$  nM [ $5 \mu\text{g/mL}$ ]). Sotrovimab inhibits an undefined step that occurs after virus attachment and prior to fusion of the viral and cell membranes. The Fc domain of sotrovimab includes M428L and N434S amino acid substitutions (LS modification) that extend antibody half-life, but do not impact wild-type Fc-mediated effector functions in cell culture.

### Antiviral Activity

The neutralization activity of sotrovimab against SARS-CoV-2 (isolate WA1/2020) was measured in a concentration response model using cultured Vero E6 cells. Sotrovimab neutralized SARS-CoV-2 with an average  $EC_{50}$  value of 0.67 nM (100.1 ng/mL).

Sotrovimab demonstrated cell culture Fc $\gamma$ R activation using Jurkat reporter cells expressing Fc $\gamma$ RIIa (low-affinity R131 and high affinity H131 alleles), Fc $\gamma$ RIIIa (low-affinity F158 and high-affinity V158 alleles), and Fc $\gamma$ RIIb. Sotrovimab exhibited antibody-dependent cell-mediated cytotoxicity (ADCC) in cell culture using isolated human natural killer (NK) cells following engagement with target cells expressing spike protein. Sotrovimab also elicited antibody-dependent cellular phagocytosis (ADCP) in cell-based assays using CD14<sup>+</sup> monocytes targeting cells expressing spike protein.

### Antibody Dependent Enhancement (ADE) of Infection

The risk that sotrovimab could mediate viral uptake and replication by immune cells was studied in U937 cells, primary human monocytic dendritic cells, and peripheral blood mononuclear cells. This experiment did not demonstrate productive viral infection in immune cells exposed to SARS-CoV-2 in the presence of concentrations of sotrovimab from 1-fold down to 1000-fold below the  $EC_{50}$  value.

The potential for ADE was also evaluated in a hamster model of SARS-CoV-2 using sotrovimab. Intraperitoneal administration prior to inoculation resulted in a dose-dependent improvement in all measured outcomes (body weight, total viral RNA in the lungs, or infectious virus levels based on TCID<sub>50</sub> measurements). No evidence of enhancement of disease was observed at any dose evaluated, including sub-neutralizing doses down to 0.05 mg/kg.

### Antiviral Resistance

There is a potential risk of treatment failure due to the development of viral variants that are resistant to sotrovimab.

*Cell Culture Studies:* Spike protein amino acid substitution E340A emerged in cell culture selection of resistant virus and had a  $>100$ -fold reduction in activity in a pseudotyped virus-like particle (VLP) assay. This substitution is in the conserved epitope of sotrovimab, which is comprised of 23 amino acids. Pseudotyped VLP assessments in cell culture were performed using Wuhan-Hu-1, Omicron BA.1, and Omicron BA.2 spike proteins. The epitope amino acid substitutions P337H/K/L/N/R/T, E340A/I/K/G/Q/S/V, T345P, K356T, and L441N in the Wuhan-Hu-1 spike, conferred reduced susceptibility to sotrovimab based on observed fold-increase in  $EC_{50}$  value shown in parentheses: P337H (5.1), P337K ( $>304$ ), P337L ( $>192$ ), P337N (5.6), P337R ( $>192$ ), P337T (10.6), E340A ( $>100$ ), E340G (18.2), E340I ( $>190$ ), E340K ( $>297$ ), E340Q ( $>50$ ), E340S (68), E340V ( $>200$ ), T345P (225), K356T (5.9), and L441N (72). Epitope substitutions P337H

(>631), K356T (>631), P337S (>609), E340D (>609), and V341F (5.9) in the Omicron BA.1 spike variant, and P337H (>117), P337S (>117), P337T (>117), E340D (>117), E340G (>117), K356T (>117), and K440D (5.1) in the Omicron BA.2 spike variant conferred reduced susceptibility to sotrovimab based on the observed fold-increase in EC<sub>50</sub> value shown in parenthesis relative to each spike viral variant.

Table 2 provides cell culture neutralization data for SARS-CoV-2 variants. The clinical relevance of the fold reductions in susceptibility >5 is unknown. There are no data evaluating variants with fold reductions >5 in randomized controlled clinical studies.

**Table 2. Sotrovimab Neutralization Data for SARS-CoV-2**

<b>SARS-CoV-2 Variant</b>		<b>Key Substitutions Tested<sup>a</sup></b>	<b>Fold Reduction in Susceptibility<sup>b</sup></b>	
<b>Lineage</b>	<b>WHO Nomenclature</b>		<b>Pseudotyped VLP</b>	<b>Authentic Virus</b>
B.1.1.7	Alpha	N501Y	No change	No change
B.1.351	Beta	K417N+E484K+N501Y	No change	No change
P.1	Gamma	K417T+E484K+N501Y	No change	No change
B.1.617.2	Delta	L452R+T478K	No change	No change
AY.1 and AY.2	Delta [+K417N]	K417N+L452R+T478K	No change	Not tested
AY.4.2	Delta [+]	L452R+T478K	No change	Not tested
B.1.427/B.1.429	Epsilon	L452R	No change	Not tested
B.1.526	Iota	E484K	No change	Not tested
B.1.617.1	Kappa	L452R+E484Q	No change	No change
C.37	Lambda	L452Q+F490S	No change	Not tested
B.1.621	Mu	R346K+E484K+N501Y	No change	Not tested
B.1.1.529/BA.1	Omicron	G339D+S371L+S373P+S375F+K417N+N440K+G446S+S477N+T478K+E484A+Q493R+G496S+Q498R+N501Y+Y505H	No change	No change
BA.1.1	Omicron	G339D+R346K+S371L+S373P+S375F+K417N+N440K+G446S+S477N+T478K+E484A+Q493R+G496S+Q498R+N501Y+Y505H	No change	No change
BA.2	Omicron	G339D+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+S477N+T478K+E484A+Q493R+Q498R+N501Y+Y505H	16	15.7 <sup>c</sup>
BA.2.12.1	Omicron	G339D+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+L452Q+S477N+T478K+E484A+Q493R+Q498R+	16.6	25.1 <sup>c</sup>



		N501Y+Y505H		
BA.2.75	Omicron	G339H+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+G446S+N460K+S477N+T478K+E484A+Q498R+N501Y+Y505H	8.3	Not tested
BA.2.75.2	Omicron	G339H+R346T+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+G446S+N460K+S477N+T478K+E484A+F486S+Q498R+N501Y+Y505H	10	Not tested
BA.3	Omicron	G339D+S371F+S373P+S375F+D405N+K417N+N440K+G446S+S477N+T478K+E484A+Q493R+Q498R+N501Y+Y505H	7.3	Not tested
BA.4	Omicron	G339D+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+L452R+S477N+T478K+E484A+F486V+Q498R+N501Y+Y505H	21.3	48.4 <sup>c</sup>
BA.4.6	Omicron	G339D+R346T+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+L452R+S477N+T478K+E484A+F486V+Q498R+N501Y+Y505H	57.9	Not tested
BA.5	Omicron	G339D+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+L452R+S477N+T478K+E484A+F486V+Q498R+N501Y+Y505H	22.6	21.6 <sup>c</sup>
BF.7/BA.5.2.6	Omicron	G339D+R346T+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+L452R+S477N+T478K+E484A+F486V+Q498R+N501Y+Y505H	74.2	Not tested
BN.1	Omicron	<u>G339H+R346T+K356T+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+G446S+N460K+S477N+T478K+E484A+F490S+Q498R+</u>	778	Not tested

		<u>N501Y+Y505H</u>		
BQ.1	Omicron	G339D+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+K444T+L452R+N460K+S477N+T478K+E484A+F486V+Q498R+N501Y+Y505H	28.5	Not tested
BQ.1.1	Omicron	G339D+R346T+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+K444T+L452R+N460K+S477N+T478K+E484A+F486V+Q498R+N501Y+Y505H	94	Not tested
XBB/XBB.1	Omicron	G339H+R346T+L368I+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+V445P+G446S+N460K+S477N+T478K+E484A+F486S+F490S+Q498R+N501Y+Y505H	6.5	Not tested
XBB.1.5	Omicron	G339H+R346T+L368I+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+V445P+G446S+N460K+S477N+T478K+E484A+F486P+F490S+Q498R+N501Y+Y505H	11.3	33.3 <sup>c</sup>
XD	None <sup>d</sup>	G339D+S371L+S373P+S375F+K417N+N440K+G446S+S477N+T478K+E484A+Q493R+G496S+Q498R+N501Y+Y505H	Not tested	No change

<sup>a</sup> Substitutions in the spike receptor binding domain relative to wild-type are listed.

<sup>b</sup> Based on EC<sub>50</sub> fold change compared to wild-type. No change: ≤5-fold change in EC<sub>50</sub> value compared to wild-type.

<sup>c</sup> Sotrovimab inhibited authentic virus isolates of Omicron BA.2, BA.2.12.1, BA.4, BA.5, and XBB.1.5 lineages with maximum percentage inhibition in the range of 80% to 100%.

<sup>d</sup> Variant has not been named by the WHO.

*Clinical Studies:* SARS-CoV-2 variants of concern or variants of interest (VOC/VOI) were detected in participants enrolled in COMET-ICE (Table 3).

**Table 3. SARS-CoV-2 VOC/VOI Detected at ≥2% Prevalence in Sotrovimab-Treated Participants**

<b>Clinical Study</b>	<b>VOC/VOI</b>	<b>Prevalence, % (n/N)<sup>a</sup></b>	<b>Participants Meeting Primary Clinical Endpoint<sup>b</sup></b>
COMET-ICE	Alpha (B.1.1.7)	10% (35/338)	1
	Epsilon (B.1.427/B.1.429)	5% (16/338)	1
	Gamma (P.1)	3% (9/338)	0

<sup>a</sup> n = number of sotrovimab-treated participants with the designated VOC/VOI; N = total number of sotrovimab-treated participants with SARS-CoV-2 spike sequence results.

<sup>b</sup> The primary clinical endpoint for progression was defined as hospitalization for >24 hours for acute management of any illness or death from any cause through Day 29.

SARS-CoV-2 viruses with baseline and treatment-emergent substitutions at amino acid positions associated with reduced susceptibility to sotrovimab in cell culture were observed in COMET-ICE (Table 4). Of the 32 sotrovimab-treated participants with a substitution detected at amino acid positions 337 and/or 340 at any visit baseline or post-baseline, only 1 met the primary endpoint for progression of hospitalization for >24 hours for acute management of any illness or death from any cause through Day 29. This participant had E340K detected post-baseline and was infected with the Epsilon variant of SARS-CoV-2.

**Table 4. Baseline and Treatment-Emergent Substitutions Detected in Sotrovimab-Treated Participants at Amino Acid Positions Associated with Reduced Susceptibility to Sotrovimab**

<b>Clinical Study</b>	<b>Baseline<sup>a</sup></b>		<b>Treatment-Emergent<sup>b</sup></b>	
	<b>Substitutions</b>	<b>Frequency, % (n/N)</b>	<b>Substitutions</b>	<b>Frequency, % (n/N)</b>
COMET-ICE	P337H, E340A	1% (4/307)	P337L/R, E340A/K/V	14% (24/170) <sup>c</sup>

<sup>a</sup> n = number of sotrovimab-treated participants with a baseline substitution detected at spike amino acid positions 337 or 340; N = total number of sotrovimab-treated participants with baseline sequence results.

<sup>b</sup> n = number of sotrovimab-treated participants with treatment-emergent substitutions detected at spike amino acid positions 337 or 340; N = total number of sotrovimab-treated participants with paired baseline and post-baseline sequence results.

<sup>c</sup> Four participants with a post-baseline substitution at P337 or E340 and lacking a baseline sequence are not included.

### Immune Response Attenuation

There is a theoretical risk that antibody administration may attenuate the endogenous immune response to SARS-CoV-2 and make patients more susceptible to re-infection.

## **12.6 Immunogenicity**

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies may be misleading.

Treatment-emergent anti-drug antibodies (ADAs) to sotrovimab were detected in 13% (65/513) of participants, through week 24, in the COMET-ICE study. None of the participants with confirmed treatment-emergent ADAs had neutralizing antibodies against sotrovimab.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Carcinogenesis, mutagenesis, and reproductive toxicology studies with sotrovimab have not been conducted.

In a toxicology study in monkeys, sotrovimab had no adverse effects when administered intravenously.

In tissue cross reactivity studies using human and monkey adult tissues, no binding of clinical concern was detected for sotrovimab.

### **13.2 Animal Toxicology and/or Pharmacology**

In a Syrian Golden hamster model of SARS-CoV-2 infection, antiviral activity was demonstrated using a single dose of sotrovimab which was administered intraperitoneally at 24- or 48-hours prior to infection. Animals receiving 5 mg/kg or more of the antibody showed a significant improvement in body weight loss and significantly decreased total lung SARS-CoV-2 viral RNA compared to vehicle only and control antibody-treated animals. Levels of virus in the lung (as measured by TCID<sub>50</sub>) were significantly decreased versus controls in hamsters receiving 0.5 mg/kg or more of the antibody.

Protection was also observed in the Syrian Golden hamster model using the SARS-CoV-2 B.1.351 (Beta, South Africa origin) variant. Significant reductions in total and replication competent virus were observed on Day 4 post-infection in animals receiving a single intraperitoneal dose of 0.5, 2, 5, or 15 mg/kg sotrovimab compared to isotype control antibody-treated animals.

## **14 CLINICAL STUDIES**

The clinical data supporting this EUA are based on the analysis of the Phase 1/2/3 COMET-ICE trial (NCT04545060) with supporting data from the Phase 3 COMET-TAIL trial (NCT04913675).

### COMET-ICE (Study 214367)

COMET-ICE was a randomized, multi-center, double-blind, placebo-controlled trial studying sotrovimab for the treatment of subjects with mild-to-moderate COVID-19 (subjects with COVID-19 symptoms who were not hospitalized). Eligible subjects were 18 years of age and older with at least one of the following comorbidities: diabetes,

obesity (BMI  $\geq 30$ ), 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 trial included symptomatic subjects with SARS-CoV-2 infection as confirmed by local laboratory tests and/or point of care tests and symptom onset within 5 days of enrollment. The study was conducted when the wild-type Wuhan-Hu-1 virus was predominant, with the highest frequency of variants being Alpha and Epsilon [see *Microbiology (12.4)*]. Subjects with severe COVID-19 requiring supplemental oxygen or hospitalization and severely immunocompromised subjects were excluded from the trial.

A total of 1,057 eligible subjects were randomized to receive a single 500-mg infusion of sotrovimab (n = 528) or placebo (n = 529) over 1 hour (Intent to Treat [ITT] population at Day 29). At baseline, the median age was 53 years (range:17 to 96); 20% of subjects were 65 years of age or older and 11% were over 70 years of age; 46% of subjects were male; 87% were White, 8% Black or African American, 4% Asian, 65% Hispanic or Latino. Fifty-nine percent of subjects received sotrovimab or placebo within 3 days of COVID-19 symptom onset and 41% within 4 to 5 days. The four most common pre-defined risk factors or comorbidities were obesity (63%), 55 years of age or older (47%), diabetes requiring medication (22%), and moderate-to-severe asthma (17%). Overall, baseline demographic and disease characteristics were well balanced between the treatment arms.

The primary endpoint, progression of COVID-19 at Day 29, was reduced by 79% (adjusted relative risk reduction) in recipients of sotrovimab versus placebo. Table 5 provides the results for the primary and key secondary endpoint of COMET-ICE.

**Table 5. Efficacy Results in Adults with Mild-to-Moderate COVID-19 in COMET-ICE at Day 29**

	<b>Sotrovimab 500 mg n = 528</b>	<b>Placebo n = 529</b>
<b>Progression of COVID-19 (defined as hospitalization for &gt;24 hours for acute management of any illness or death from any cause) (Day 29)<sup>a</sup></b>		
Proportion (n, %)	6 (1.1%)	30 (5.7%)
Adjusted Relative Risk Reduction (95% CI)	79% (50%, 91%)	
<b>All-cause mortality (up to Day 29)</b>		
Proportion (n, %)	0	2 (<1%)

<sup>a</sup> The determination of primary efficacy was based on a planned interim analysis of 583 subjects, which had similar findings to those seen in the full population above. The adjusted relative risk reduction was 85% with a 97.24% CI of (44%, 96%) and p-value = 0.002.

Within the subset of the ITT population who had a central laboratory confirmed, virologically quantifiable nasopharyngeal swab at Day 1 and Day 8 (n = 639), the mean decline in viral RNA levels from baseline to Day 8 was greater in subjects treated with sotrovimab (-2.610 log<sub>10</sub> copies/mL) compared to that in subjects treated with placebo (-2.358); mean difference = -0.251, 95% CI: (-0.415, -0.087).

## COMET-TAIL (Study 217114)

COMET-TAIL was a randomized, multi-center, open label trial which evaluated the efficacy, safety, and tolerability of sotrovimab for the treatment of subjects with mild-to-moderate COVID-19 (subjects with COVID-19 symptoms who were not hospitalized). Eligible subjects were 12 years of age or older with at least one of the following comorbidities: diabetes, obesity (BMI  $\geq$ 85<sup>th</sup> percentile for age/gender based on Centers for Disease Control and Prevention [CDC] growth charts for adolescents or BMI  $\geq$ 30 for subjects  $\geq$ 18 years old), chronic kidney disease, congenital heart disease, congestive heart failure (for subjects  $\geq$ 18 years old), chronic lung diseases, sickle cell disease, neurodevelopmental disorders, immunosuppressive disease or receiving immunosuppressive medications, or chronic liver disease; or were 55 years of age or older regardless of comorbidities. The trial included symptomatic subjects with SARS-CoV-2 infection as confirmed by local laboratory tests and/or point of care tests and symptom onset within 7 days of enrollment. Subjects with severe COVID-19 requiring supplemental oxygen or hospitalization were excluded from the trial.

The ITT population consisted of 385 subjects randomized to receive a single 500-mg IV infusion of sotrovimab over 15 minutes. The primary analysis population, which excluded 7 subjects because they were fully vaccinated and immunocompetent (key inclusion/exclusion violation), consisted of 378 subjects.

In the primary analysis population at baseline, the median age was 51 years (range:15 to 90, including 2 subjects under 18 years); 25% of subjects were 65 years of age or older and 8% were over 75 years of age; 42% of subjects were male; 96% were White and 4% were Black or African American; 83% were Hispanic or Latino. Forty-eight percent (48%) of subjects received sotrovimab within 3 days of COVID-19 symptom onset, 37% within 4 to 5 days, and 14% within 6 to 7 days. The four most common pre-defined risk factors or comorbidities were obesity (63%), 55 years of age or older (42%), chronic lung disease (16%), and diabetes requiring medication (13%).

In the primary analysis population, 5 (1.3%) of 378 subjects had progression to COVID-19 defined as hospitalization for >24 hours for acute management of any illness or death due to any cause through Day 29. No deaths were reported through Day 29.

## **16 HOW SUPPLIED/STORAGE AND HANDLING**

### How Supplied

Sotrovimab injection 500 mg (62.5 mg/mL) is a sterile, preservative-free, clear, colorless or yellow to brown solution supplied in a carton containing one single-dose glass vial with a rubber vial stopper (not made with natural rubber latex) and a flip-off cap (NDC 0173-0901-86).

### Storage and Handling

Sotrovimab is preservative-free. Discard unused portion.

Store unopened vials refrigerated at 2°C to 8°C (36°F to 46°F) in original carton. Do not freeze or shake. Protect from light.

The concentrate for solution of sotrovimab in the vial is preservative-free and requires dilution prior to IV administration. The diluted infusion solution of sotrovimab should be administered immediately. If immediate administration is not possible, store the diluted

infusion solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or up to 6 hours at room temperature (up to 25°C [up to 77°F]) including transportation and infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 15 minutes prior to administration.

## **17 PATIENT COUNSELING INFORMATION**

As a healthcare practitioner, you must communicate to the patient and/or caregiver information consistent with the “FACT SHEET FOR PATIENTS AND CAREGIVERS” and provide them with a copy of this Fact Sheet prior to administration of sotrovimab. However, if providing this information will delay the administration of sotrovimab to a degree that would endanger the life of a patient, the information must be provided to the parent and/or caregiver as soon as feasible after sotrovimab administration.

### Hypersensitivity Reactions

Inform patients that 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, advise patients to alert healthcare provider immediately. Inform patients that hypersensitivity reactions occurring more than 24 hours after the infusion have also been reported with the use of SARS-CoV-2 monoclonal antibodies and to alert their healthcare provider immediately if signs and symptoms of hypersensitivity occur [see *Warnings and Precautions (5.1)*].

### Pregnancy Registry

Advise patients that there is a pregnancy registry that monitors pregnancy outcomes in individuals exposed to sotrovimab during pregnancy [see *Use in Specific Populations (8.1)*].

## **18 MANUFACTURER INFORMATION**

Trademark is owned by or licensed to the GSK group of companies.

Manufactured by **GlaxoSmithKline LLC**

Philadelphia, PA 19104, U.S. License No. 1727

Distributed by **GlaxoSmithKline**

Durham, NC 27701

©2023 GSK group of companies or its licensor.

STR:9FS-HCP

Revised: March 2023

DETACH HERE AND GIVE FACT SHEET TO PATIENT, PARENT OR CAREGIVER.

-----  
-----

## **FACT SHEET FOR PATIENTS AND PARENTS/CAREGIVERS**

### **EMERGENCY USE AUTHORIZATION (EUA) OF SOTROVIMAB FOR THE TREATMENT OF CORONAVIRUS DISEASE 2019 (COVID-19)**

You are being given this fact sheet because your healthcare provider believes it is necessary to provide you or your child with sotrovimab for the treatment of adults and children (12 years of age and older weighing at least 88 pounds [40 kg]) with positive results of direct SARS-Co-V-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death. This fact sheet contains information to help you understand the potential risks and potential benefits of receiving sotrovimab, which you or your child have received or may receive.

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to make sotrovimab available during the COVID-19 pandemic (for more details about an EUA please see “**What is an Emergency Use Authorization?**” at the end of this document). Sotrovimab is not an FDA-approved medicine in the United States. Read this Fact Sheet for information about sotrovimab. Talk to your healthcare provider about your options or if you have any questions. It is your choice for you or your child to receive sotrovimab or stop it at any time.

#### **WHAT IS COVID-19?**

COVID-19 is caused by a virus called a coronavirus. People can get COVID-19 through close contact with another person who has the virus.

COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can happen and may cause some of your or your child’s other medical conditions to become worse. Older people and people of all ages with severe, long lasting (chronic) medical conditions like heart disease, lung disease, and diabetes for example, seem to be at higher risk of being hospitalized for COVID-19.

#### **WHAT IS SOTROVIMAB?**

Sotrovimab is an investigational medicine used for the treatment of adults and children (12 years of age and older weighing at least 88 pounds [40 kg]) with positive results of direct SARS-Co-V-2 viral testing, and who are at high risk of progression to severe COVID-19, including hospitalization or death.

Sotrovimab is investigational because it is still being studied. There is limited information about the safety and effectiveness of using sotrovimab to treat people with mild-to-moderate COVID-19.

The FDA has authorized the emergency use of sotrovimab for the treatment of adults and children (12 years of age and older weighing at least 88 pounds [40 kg]) with positive results of direct SARS-Co-V-2 viral testing, and who are at high risk of progression to severe COVID-19, including hospitalization or death, under an EUA. For more information on EUA, see the “**What is an Emergency Use Authorization (EUA)?**” section at the end of this Fact Sheet.

Sotrovimab is not authorized for use in people who:

- are hospitalized due to COVID-19, **or**



- require oxygen therapy or breathing support due to COVID-19, **or**
- are on chronic oxygen therapy or breathing support at home before their COVID-19 diagnosis, and who require an increase in the amount of oxygen they need or breathing support due to COVID-19.

## **WHAT SHOULD I TELL MY HEALTHCARE PROVIDER BEFORE I OR MY CHILD RECEIVE SOTROVIMAB?**

### **Tell your healthcare provider if you or your child:**

- have any allergies
- are pregnant or plan to become pregnant
- are breastfeeding or plan to breastfeed
- have any serious illnesses
- take any medicines including prescription, over-the-counter medicines, vitamins, and herbal products

## **HOW WILL I OR MY CHILD RECEIVE SOTROVIMAB?**

- You or your child will receive 1 dose of sotrovimab.
- Sotrovimab will be given through a vein (intravenous or IV infusion) by a healthcare provider over 15 or 30 minutes.
- You or your child will be monitored by your healthcare provider for at least 1 hour after receiving sotrovimab.

## **WHO SHOULD GENERALLY NOT RECEIVE SOTROVIMAB?**

Do not receive sotrovimab if you or your child have had a serious allergic reaction to sotrovimab or to any of the ingredients in sotrovimab. See the end of the Fact Sheet for a complete list of ingredients in sotrovimab.

## **WHAT ARE THE IMPORTANT POSSIBLE SIDE EFFECTS OF SOTROVIMAB?**

Possible side effects of sotrovimab are:

- **Allergic reactions.** Allergic reactions can happen during and after receiving sotrovimab. Tell your healthcare provider right away if you or your child develop any of the following signs and symptoms of allergic reactions: fever; difficulty breathing; low oxygen level in your blood; chills; tiredness; fast or slow heart rate; chest discomfort or pain; weakness; confusion; nausea; headache; shortness of breath; low or high blood pressure; wheezing; swelling of your lips, face, or throat; rash including hives; itching; muscle aches; dizziness; feeling faint; and sweating.

Side effects of receiving sotrovimab intravenously may include brief pain, bleeding, bruising of the skin, soreness, swelling, and possible infection at the infusion site.

Other possible side effects of sotrovimab include rash and diarrhea.

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.

## **WHAT OTHER TREATMENT CHOICES ARE THERE?**

Veklury (remdesivir) is FDA-approved for the treatment of mild-to-moderate COVID-19 in

certain adults and children. Talk with your healthcare provider to see if Veklury is appropriate for you.

Like sotrovimab, FDA may allow for the emergency use of other medicines to treat people with COVID-19. Go to <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization> for information on the emergency use of other medicines that are authorized by FDA to treat people with COVID-19. Your healthcare provider may talk with you about clinical trials for which you may be eligible.

It is your choice for you or your child to be treated or not to be treated with sotrovimab. Should you decide not to receive it or your child not to receive it, it will not change your or your child's standard medical care.

## **WHAT IF I AM PREGNANT OR BREASTFEEDING?**

There is no experience treating pregnant women or breastfeeding mothers with sotrovimab. For a mother and unborn baby, the benefit of receiving sotrovimab may be greater than the risk from the treatment. If you are pregnant or breastfeeding, discuss your options and specific situation with your healthcare provider.

### Pregnancy Exposure Registry

There is a pregnancy exposure registry for individuals who receive sotrovimab during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk with your healthcare provider about how to take part in this registry. For more information visit <https://covid-pr.pregistry.com> or call 1-800-616-3791.

## **HOW DO I REPORT SIDE EFFECTS WITH SOTROVIMAB?**

Contact your healthcare provider if you or your child have any side effects that bother you or your child or do not go away. Report side effects to **FDA MedWatch** at [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088, or call GSK at 1-866-475-2684.

## **How can I learn more about COVID-19?**

- Ask your healthcare provider
- Visit <https://www.cdc.gov/COVID19>
- Contact your local or state public health department

## **What is an Emergency Use Authorization?**

The United States FDA has made sotrovimab available under an emergency access mechanism called an Emergency Use Authorization (EUA). The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

Sotrovimab for the treatment of adults and children (12 years of age and older) weighing at least 88 pounds [40 kg]) with positive results of direct SARS-Co-V-2 viral testing, and who are at high risk of progression to severe COVID-19, including hospitalization and death, has not undergone the same type of review as an FDA-approved product. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, and available alternatives. In addition, the FDA decision is based on the totality of scientific evidence available showing that it is

reasonable to believe that the product meets certain criteria for safety, performance, and labeling and may be effective in treatment of patients during the COVID-19 pandemic.

All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic. The EUA for sotrovimab is in effect for the duration of the COVID-19 declaration justifying emergency use of sotrovimab, unless terminated or revoked (after which sotrovimab may no longer be used under the EUA).

Manufactured by **GlaxoSmithKline LLC**

Philadelphia, PA 19104, U.S. License No. 1727

Distributed by **GlaxoSmithKline**

Durham, NC 27701

©2023 GSK group of companies or its licensor.

STR:5FS-P

Revised: March 2023

## **PRINCIPAL DISPLAY PANEL**

**NDC 0173-0901-86**

**Sotrovimab**

**Injection**

**500 mg/8 mL**

**(62.5 mg/mL)**

**Rx Only**

**For intravenous infusion after further dilution.**

**Contains One 8-mL Single-Dose Vial.**

**Discard Unused Portion.**

**For Use Under Emergency Use Authorization (EUA)**

©2021 GSK group of companies or its licensor.

Product of China

Rev. 4/21

62000000058567

NDC 0173-0901-86  
Rx Only



# Sotrovimab

## injection

### 500 mg/8 mL

### (62.5 mg/mL)

For intravenous infusion after further dilution.  
Contains One 8-mL Single-Dose Vial.  
Discard Unused Portion.

**For Use Under Emergency Use  
Authorization (EUA)**

## SOTROVIMAB

sotrovimab injection, solution, concentrate

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:0173-0901
<b>Route of Administration</b>	INTRAVENOUS		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
<b>SOTROVIMAB</b> (UNII: 1MTK0BPN8V) (SOTROVIMAB - UNII:1MTK0BPN8V)	SOTROVIMAB	62.5 mg in 1 mL

## Inactive Ingredients

Ingredient Name	Strength
<b>HISTIDINE MONOHYDROCHLORIDE</b> (UNII: 1D5Q932XM6)	
<b>METHIONINE</b> (UNII: AE28F7PNPL)	
<b>POLYSORBATE 80</b> (UNII: 6OZP39ZG8H)	
<b>SUCROSE</b> (UNII: C151H8M554)	

## Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0173-0901-86	1 in 1 CARTON	05/26/2021	
1		8 mL in 1 VIAL; Type 0: Not a Combination Product		

## Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug other		05/26/2021	

**Labeler** - GlaxoSmithKline LLC (167380711)

Revised: 3/2023

GlaxoSmithKline LLC