NEW DRUG APPROVAL

Brand Name	N/A
Generic Name	sotrovimab
Drug Manufacturer	GlaxoSmithKline LLC.

New Drug Approval

FDA Approval Date: May 26, 2021
Review Designation: **Emergency Use Authorization**
Type of Review: N/A
Dispensing Restrictions: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus.

Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.

The best way to prevent and slow down transmission is to be well informed about the COVID-19 virus, the disease it causes and how it spreads. Protect yourself and others from infection by washing your hands or using an alcohol based rub frequently and not touching your face.

The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that you also practice respiratory etiquette (for example, by coughing into a flexed elbow).

Globally, over 150 million confirmed cases of COVID-19 have been reported.

Since the first reports of cases from Wuhan, a city in the Hubei Province of China, at the end of 2019, cases have been reported in all continents.

The reported case counts underestimate the overall burden of COVID-19, as only a fraction of acute infections are diagnosed and reported. Seroprevalence surveys in the United States and Europe have suggested that after accounting for potential false positives or negatives, the rate of prior exposure to SARS-CoV-2, as reflected by seropositivity, exceeds the incidence of reported cases by approximately 10-fold or more.

Efficacy

Emergency Use Authorization (EUA) for sotrovimab are based on an interim analysis from a phase 1/2/3 randomized, double-blind, placebo-controlled clinical trial 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 five days of onset of COVID-19 symptoms. The primary endpoint was progression of COVID-19 (defined as hospitalization for greater than 24 hours for acute management of any illness or death from any cause) through day 29. Hospitalization or death occurred in 21 (7%) patients who received placebo compared to 3 (1%) patients treated with sotrovimab, an 85% reduction.

Table: Interim Efficacy Results in Adults with Mild-to-Moderate COVID-19

	Sotrovimab n = 291	Placebo n = 292
Progression of COVID-19 (defined as hospitalization for >24 hours for acute management of any illness or death from any cause) (Day 29)		
Proportion (n, %)	3 (1%)	21 (7%)
Adjusted Relative Risk Reduction (97.24% CI)	85% (44%, 96%)	
p-value	0.002	
All-cause mortality (up to Day 29)		
Proportion (n, %)	0	1 (<1%)

Safety

ADVERSE EVENTS

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.

WARNINGS & 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.

CONTRAINDICATIONS

None.

Clinical Pharmacology

MECHANISMS 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 K_D = 0.21 nM) but does not compete with human ACE2 receptor binding (IC_{50} value >33.6 nM [5 µg/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.

Dose & Administration

ADULTS

Emergency Use Authorization: sotrovimab is authorized for emergency use by the US Food and Drug Administration (FDA) for the treatment of mild to moderate COVID-19 in adults and pediatric patients aged 12 years or older and at least 40 kg. 500 mg as a single intravenous infusion over 30 minutes. Administer the infusion as soon as possible after the positive test for SARS-CoV-2 and within 10 days of symptom onset.

PEDIATRICS

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.

GERIATRICS

Refer to adult dosing.

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.

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.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Sotrovimab is a sterile, preservative-free, clear, colorless or yellow to brown solution available as: Injection: 500-mg/8-mL (62.5-mg/mL) solution in a single-dose vial for intravenous infusion after dilution.