Emergency Use Authorization (EUA) for Sotrovimab 500 mg
Center for Drug Evaluation and Research (CDER) Memorandum on
Fact Sheet Update

Identifying Information

Application Type (EUA or Pre-EUA)	EUA
EUA Application Number	EUA 000100, SDN 60
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	EUA Sponsor GlaxoSmithKline Research & Development Limited 980 Great West Road Brentford Middlesex, TW8 9GS UK GSK US Point of Contact Debra H. Lake, M.S. Sr. Director Global Regulatory Affairs GlaxoSmithKline 5 Moore Drive PO Box 13398 Research Triangle Park, NC 27709-3398 Email: (b) (6) Phone: (b) (6)
Manufacturer	GlaxoSmithKline, Parma.
Submission Date	October 1, 2021
Receipt Date	October 1, 2021
Review Completion Date	October 29, 2021
OND Division / Office	Division of Antivirals (DAV)/Office of Infectious Diseases (OID)
Reviewer Name(s)/Discipline(s)	Sarita Boyd, Clinical Reviewer Kimberly Struble, Clinical Team Lead Eric Donaldson, Clinical Virology Reviewer Julian O'Rear, Clinical Virology Team Lead Debra Birnkrant, Division Director, DAV John Farley, Office Director, OID
Proprietary Name	None
Established Name/Other names used during development	Sotrovimab (VIR-7831)
Dosage Forms/Strengths	Sterile solution for injection, 500mg/8 mL vial
Therapeutic Class	SARS-CoV-2 spike protein directed human IgG1κ monoclonal antibody (mAb)
Intended Population	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

I. Review of Fact Sheet Revisions

The following proposed updates to the long version of the Fact Sheet (FS) for Healthcare Providers (HCP) were reviewed. Corresponding changes, where applicable, were made to the short version of the FS for HCP and to the FS for Patients, Parents, and Caregivers.

A. Contraindications (4)

The Applicant is proposing a contraindication in patients who have a history of anaphylaxis to sotrovimab or any of the excipients in the formulation. The FS for patients was in turn updated to include the list of excipients.

Although sotrovimab is authorized for use as a single dose, patients previously treated with sotrovimab may experience reinfection with SARS-CoV-2 and become eligible for a separate treatment course of single-dose sotrovimab. The proposal is acceptable.

B. Overall Safety Summary: Post-Authorization Experience (6.2)

The Applicant is proposing the addition of anaphylaxis specifically as an adverse reaction reported during post-authorization use of sotrovimab. A 26-year-old male in the United Arab Emirates with mild to moderate COVID-19, a positive SARS-CoV-2 test result, and risk factors of diabetes and being overweight received a single IV infusion of sotrovimab 500 mg. Soon after, he experienced generalized rash and facial swelling, which were treated with corticosteroids. Two hours later, he progressed to anaphylactic shock leading to hospitalization and treatment with epinephrine. The outcome of the event was not reported.

The current FS includes anaphylaxis as an adverse reaction reported after sotrovimab infusion in a study in hospitalized patients, a population for whom sotrovimab is not authorized. The proposed addition of Section 6.2 accurately conveys that anaphylaxis has also been observed with sotrovimab in the post-authorization outpatient setting and specifically in a patient representing the population for whom sotrovimab is authorized. Importantly, the Warning and Precaution (5.1) for Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions is unchanged and remains adequate. Overall, the proposal is acceptable.

C. Microbiology/Resistance Information (15)

The Applicant is proposing to update the Section 15: Microbiology/Resistance Information of the Fact Sheet for Healthcare Providers to include additional information regarding SARS-CoV-2 variants of concern/variants of interest. The revision provided summary data of cell culture pseudotype virus like particle assessments of sotrovimab antiviral

activity against the SARS-CoV-2 Lambda (C.37, Peru origin) and Mu (B.1.621, Brazil origin) variants, which resulted in no change in susceptibility (<5-fold reduction).

Clinical Virology reviewed the revisions and identified minor edits in the footnotes describing the Lambda (C.37, Peru origin) and Mu (B.1.621, Brazil origin) variants that were communicated to the Applicant. In addition, the Applicant identified minor inaccuracies pertaining to the fold-shifts in susceptibility of the Delta (B.1.617.2, India origin) and Kappa (B.1.617.1, India origin) variants that were corrected. The proposed revisions to the Fact Sheet for Healthcare Providers and are acceptable with edits.

II. Recommendations

The proposed revisions to the Fact Sheet for Healthcare Providers and Fact Sheet for Patients, Parents, and Caregivers are acceptable with edits.

The agreed upon FS updates do not alter the benefit-risk analysis or conclusion in the initial review to support authorization of EUA 100.

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/s/

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