Emergency Use Authorization (EUA) for REGEN-COV

Center for Drug Evaluation and Research (CDER) Memorandum

Identifying Information

Application Type (EUA or Pre-EUA) If EUA, designate whether pre-event or intra-event EUA request.	EUA
EUA Application Number(s)	91
Date of Memorandum	February 25, 2021
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	Regeneron Pharmaceuticals, Inc. Yunji Kim, PharmD Director, Regulatory Affairs Regeneron Pharmaceuticals, Inc. Mobile: (b) (6) Email: yunji.kim@regeneron.com
Manufacturer	Regeneron Pharmaceuticals, Inc.
OND Division / Office	Division of Antivirals (DAV)/Office of Infectious Diseases (OID)
Integrated Review Completion Date	November 21, 2020
Proprietary Name	REGEN-COV
Established Name/Other names used during development	casirivimab (REGN10933) and imdevimab (REGN10987)
Dosage Forms/Strengths	1200 mg intravenous (IV) casirivimab and 1200 mg IV imdevimab
Therapeutic Class	SARS-CoV-2 spike protein directed human IgG1 monoclonal antibody (mAb)

Intended Use or Need for EUA	mild to moderate coronavirus disease 2019 (COVID-19)
Intended Population(s)	treatment of mild to moderate coronavirus disease (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 risk for progressing to severe COVID-19 illness and/or hospitalization

Emergency Use Authorization (EUA) 91 authorizes the emergency use of REGEN-COV 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 progressing to severe COVID-19 and/or hospitalization. This memorandum provides a brief summary of changes to the Letter of Authorization for EUA 91.

Under section 564(g) of the Federal Food, Drug & Cosmetic Act, the Agency must periodically review the circumstances and appropriateness of an EUA. The Agency may revise an EUA, for example, if circumstances warrant revision to protect the public health or safety.

On February 3, 2021, FDA issued the Letter of Authorization (LOA) for EUA 91, which included a condition to the authorization requiring Regeneron to submit instructional and educational materials to the Agency for review and concurrence prior to initial dissemination of such materials, or when making revisions to instructional and educational materials previously authorized. Upon further consideration, FDA believes that making instructional and educational materials available in an expedient manner, when such materials are necessary to meet public health needs and on condition that these materials are consistent with the terms and conditions of the authorization, including authorized labeling, will facilitate the appropriate use of the authorized REGEN-COV. Section 564 of the FD&C Act, including condition E as revised below, details mechanisms by which FDA may address any disseminated instructional or educational materials that are inconsistent with the terms and conditions of the authorization, including the authorized labeling.

As such, FDA is revising condition E, as detailed below, to no longer require prior Agency review and concurrence of instructional and educational materials, or revisions to instructional and educational materials previously authorized.

E. Regeneron may develop and disseminate instructional and educational materials (e.g., materials providing information on product administration and/or patient monitoring) that are consistent with the authorized emergency use of REGEN-COV as described in the letter of authorization and authorized labeling, without FDA's review and concurrence, when

necessary to meet public health needs. Any instructional and educational materials that are inconsistent with the authorized labeling for REGEN-COV are prohibited. Should the Agency become aware of any instructional or educational materials that are inconsistent with the authorized labeling for REGEN-COV, the Agency will require Regeneron to cease distribution of such instructional or educational materials.

The Letter of authorization will also be revised to include a non-substantive edit to condition H, as follows:

H. Regeneron will submit information to the Agency within three working days of receipt of any information concerning any batch of REGEN-COV (whether the batch is distributed or not), as follows: (1) information concerning any incident that causes the product or its labeling to be mistaken for, or applied to, another article; and (2) information concerning any microbiological contamination, or any significant chemical, physical, or other change in deterioration in the product, or any failure of one or more batches of the product to meet the established specifications. Regeneron will include in its notification to the Agency whether the batch, or batches, in question will be recalled. If FDA requests that these, or any other batches, at any time, be recalled, Regeneron must recall them.

Lastly, SARS-CoV-2 is evolving as it spreads through the human population, resulting in the emergence of multiple variants. A new virus variant of SARS-CoV-2 has one or more mutations that differentiate it from the original Wuhan isolate (Wuhan-Hu1) or predominant virus variants already circulating in the general population. Variants of SARS-CoV-2 are identified by genomic sequences that contain mutation(s) in the RNA genome, which could result in amino acid substitutions, insertions, and/or deletions in viral proteins. Mutations in genomic regions encoding for viral proteins that are targeted by therapeutics are of particular concern as the mutations may result in resistance to these therapies. Consequently, FDA is revising the LOA to include two new conditions on the monitoring and assessment of emerging global viral variants, as follows:

N. Regeneron will establish a process for monitoring genomic database(s) for the emergence of global viral variants of SARS-CoV-2. A summary of Regeneron's process should be submitted to the Agency as soon as practicable, but no later than 30 calendar days of the issuance of this letter, and within 30 calendar days of any material changes to such process. Regeneron will provide reports to the Agency on a monthly basis summarizing any findings as a result of its monitoring activities and, as needed, any follow-up assessments planned or conducted.

O. FDA may require Regeneron to assess the activity of the authorized REGEN-COV against any global SARS-CoV-2 variant(s) of interest (e.g., variants that are prevalent or becoming prevalent that harbor substitutions in the target protein or in protein(s) that interact with the target

protein). Regeneron will perform the required assessment in a manner and timeframe agreed upon by Regeneron and the Agency. Regeneron will submit to FDA a preliminary summary report immediately upon completion of its assessment followed by a detailed study report within 30 calendar days of study completion. Regeneron will submit any relevant proposal(s) to revise the authorized labeling based on the results of its assessment, as may be necessary or appropriate based on the foregoing assessment.

Regulatory Conclusion:

Consistent with section 564(g) of the FD&C Act, FDA will be re-issuing the Letter of Authorization for EUA 91, dated February 9, 2021, in its entirety to include the revisions detailed above. These revisions, among other things, revise the process for the development and dissemination of instructional and educational materials and facilitate the Agency's evaluation of any emerging global viral variants, including the assessment and potential impact on the authorized REGEN-COV.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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