

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: October 27, 2022

TO: Administrative files for the Emergency Use Authorizations for baricitinib (EUA 092), Actemra (EUA 099), EVUSHELD (EUA 104), PAXLOVID (EUA 105), Lagevrio (EUA 108), and bebtelovimab (EUA 111)

Subject: Summary Basis for Revising Certain Conditions on Printed, Advertising and Promotional Materials

Background

Under section 564 of the Federal Food, Drug & Cosmetic Act (FD&C Act), the FDA may, pursuant to a declaration by the Health and Human Services Secretary based on one of four types of determinations, authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an Emergency Use Authorization (EUA), the FDA must determine that-

- Based on the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is **reasonable** to believe that –
 - the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; and
 - that the known and potential benefits of the product, when used to treat, diagnose or prevent such disease or condition, outweigh the known and potential risks for the product;
- There are no adequate, approved, and available alternatives.

When issuing an EUA, the Agency will establish conditions on an authorization deemed necessary or appropriate to protect the public health.¹ For example, the Agency will include conditions requiring that health care professionals administering, and individuals to whom the product is administered, be informed of certain information regarding the authorized product. The Agency will also establish conditions on the monitoring and reporting of adverse events related to the emergency use of the product. Under the statutory provisions for EUAs, the Agency may also establish conditions on advertisements and other promotional descriptive printed matter that relate to the emergency use of the authorized product.²

¹ See section 564(e) of the FD&C Act.

² See section 564(e)(4) of the FD&C Act.

The statutory criteria for issuance of an EUA set forth a regulatory and scientific standard that is different from the standard required for FDA's approval of a drug.³ In many instances, an EUA sponsor continues to develop the drug as a medical countermeasure in parallel with the drug being available under EUA for such investigational use. The flexibility of the EUA statutory provisions is essential to preparing for and responding to a chemical, biological, radiological, or nuclear emergency (CBRN).

To date, the Center for Drug Evaluation and Research (CDER) has included the following condition in the Letter of Authorization for COVID-19 therapeutics⁴ relating to "Printed Matter, Advertising, and Promotional Materials":

No descriptive printed matter, advertising, or promotional materials relating to the use of Drug X under this authorization may represent or suggest that Drug X is safe or effective when used for <<authorized use>>.

This condition, in combination with other conditions on advertising and promotion currently included in EUAs for COVID-19 therapeutics, already authorize the dissemination of product-specific, truthful, and non-misleading information relating to the use of the product when consistent with the authorized labeling. Current conditions on advertising and promotional materials included in EUAs for COVID-19 therapeutics require that any such materials clearly and conspicuously state that the product (or use) is not FDA-approved, but rather has been authorized for such use for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked.

CDER was recently made aware that there may be benefit in clarifying the condition referenced above for EUA sponsors that wish to include in promotional materials information about the safety and efficacy data that supported the issuance of a particular EUA -- for example, in promotional materials disseminated to health care providers and patients. CDER has considered this and has determined that it is appropriate to make clarifying revisions to the above-referenced EUAs as further described below.

Revisions to Condition(s) on Advertising and Promotion

The Agency's understanding of COVID-19 and its impact on the public health has greatly increased during the COVID-19 public health emergency. As we've observed, the epidemiological landscape for COVID-19, specifically with emerging viral variants of SARS-CoV-2, has shifted multiple times and in a few instances, relatively quickly. In addition, the rates of infection and public health impact of the virus continues to change. Each of these factors has contributed to a shifting clinical context which healthcare providers and patients, alike, should be

³ FDA approval of a drug requires, in part, substantial evidence of effectiveness and a demonstration of safety. See section 505(d) of the FD&C Act (21 USC 355(d)).

⁴ For the purposes of this memo, the term "COVID-19 therapeutics" refers to drugs authorized for the prevention or treatment of COVID-19 under the recommendation by CDER scientific and regulatory staff.

aware; underscoring the importance for accurate and non-misleading information on the authorized COVID-19 therapeutics being available to advance the public health.

While the authorized labeling for an EUA should serve as the primary resource for information on the authorized product, dissemination of truthful and non-misleading printed matter, advertising, and promotional materials containing scientific information related to the authorized use of the product, when consistent with the terms and conditions of the respective authorization, can further enhance the public's awareness of and understanding on the authorized COVID-19 therapeutic.

As such, the Agency believes that it is appropriate⁵ to revise certain conditions on "Printed Matter, Advertising, and Promotion" in the currently authorized EUAs for COVID-19 therapeutics to replace the condition referenced above with the following language:

Company A may disseminate descriptive printed matter, advertising, and promotional materials relating to the emergency use of DRUG X that provide accurate descriptions of safety results and efficacy results on a clinical endpoint(s) from the clinical trial(s) summarized in the authorized labeling. Such materials must include any limitations of the clinical trial data as described in the authorized labeling. Company A may not imply that DRUG X is FDA approved by making statements such as "DRUG X is safe and effective for <<authorized use>>."

This section in the respective LOAs will also be revised to require that such materials be submitted to the Agency for consideration at least 14 calendar days prior to initial dissemination or first use.⁶

The Agency has determined that the revisions described above are appropriate to protect the public health or safety. These revisions clarify that the inclusion of accurate descriptions of safety and efficacy information that underly the issuance of a particular EUA in printed matter, advertising and promotional materials is authorized. Additionally, the submission of these materials to the Agency prior to initial dissemination or first use will provide CDER the opportunity to provide feedback on the submitted materials, as appropriate, to ensure consistency with the terms and conditions of the EUA, including the authorized labeling.

As noted above, FDA's authorization of a drug for emergency use under an EUA is not the same as FDA approval. When issuing an EUA, the Agency makes scientifically-based regulatory determinations on the known and potential benefits and risks of a product based on the totality of scientific information available during, or when there is a significant potential for a CBRN emergency. As such, there may be uncertainties regarding the safety and effectiveness data supporting an EUA for COVID-19 therapeutics. Accordingly, the Agency is also clarifying that printed, advertising and promotional materials need to include a description of any limitations of

⁵ See section 564(g)(2)(C) of the FD&C Act.

⁶ FDA's intention is to prioritize feedback to sponsors of EUAs during the 14-day period when significant issues are identified.

the clinical trial data, consistent with the limitations described in the authorized labeling.⁷ The inclusion of this information, along with other information required under the conditions on printed matter, advertising and promotional materials, is necessary to facilitate health care providers and patients in making informed decisions on the use of the authorized COVID-19 therapeutics.

The Agency will continue to assess the circumstances and appropriateness of each EUA covering an authorized COVID-19 therapeutic and will make additional revisions, when appropriate.

**Peter P.
Stein -S**

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Peter Stein, M.D.
Director
Office of New Drugs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

⁷ See section 564(e)(1)(A)(i)(II) and section 564(e)(1)(A)(ii)(II)

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/s/

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