



الهيئة العامة للغذاء والدواء

Saudi Food & Drug Authority

Medicinal Products Authorization During Emergency

Draft

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Medicinal Products Authorization During Emergency

Draft

Saudi Food & Drug Authority
Drug Sector

Please send your comments or suggestions before June 12, 2020

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Saudi Food and Drug Authority

Vision and Mission

Vision

To be a leading international science-based regulator to protect and promote public health

Mission

Protecting the community through regulations and effective controls to ensure the safety of food, drugs, medical devices, cosmetics, pesticides and feed



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1. INTRODUCTION

This guidance explains the procedures to authorize the emergency use of certain medicinal products when there are no adequate, approved, and available alternatives in order to strengthen the national preparedness for public health including emerging infectious disease.

Ministry of Health (MOH) is responsible for determines that there is a public health emergency or a significant potential for a public health emergency that affects, or has a significant potential to affect national security. After declaration the pandemic circumstances by MOH, the SFDA may authorize the emergency use of an unapproved product or an unapproved use of an approved product, provided that other statutory criteria are met.

Establishing this procedure allows the SFDA to facilitate the availability of unapproved uses of medicinal products to respond to the emergencies.

It gives the opportunity to different stakeholders such as pharmaceutical companies, health entities (hospitals), government sponsors to request this procedure to participate in promoting the public health during pandemic circumstances.

2. SCOPE

This procedure applicable to

- SFDA- unapproved medicinal products or
- SFDA - unapproved use of an approved medicinal products (off-label) for certain emergency circumstances.



3. CRITERIA FOR ISSUANCE

SFDA may issue an emergency authorization only if the following four criteria for issuance have been met:

a) Serious or Life-Threatening Disease or Condition

b) Evidence of Effectiveness

Medical products that may be considered for an emergency use authorization are those that "may be effective" to prevent, diagnose, or treat serious or life-threatening diseases or conditions.

For the types of evidence that SFDA may consider and that should be submitted to support a request for an emergency use authorization are discussed, please refer to Section (1) of **5.1 Information Recommendation**.

The "may be effective" standard provides a lower level of evidence than the "effectiveness" standard for product approvals. SFDA intends to assess the potential effectiveness of a possible product on a case-by-case basis using a risk-benefit analysis, as explained below.

c) Risk-Benefit Analysis

A product may be considered for an emergency use authorization if the SFDA determines that the known and potential benefits of the product, when used to diagnose, prevent, or treat the identified disease or condition, outweigh the known and potential risks of the product.

In determining whether the known and potential benefits of the product outweigh the known and potential risks, SFDA intends to look at the totality of the scientific evidence to make an overall risk-benefit determination. Such evidence, which could arise from a variety of sources, may include (but is not limited to): results of local and international clinical trials, in vivo efficacy data from animal models, and in vitro data, available for SFDA consideration. SFDA will also assess the quality and quantity of the available evidence, given the current state of scientific knowledge.



d) No alternatives

For SFDA to issue an emergency use authorization, there must be no adequate, approved, and available alternative to the candidate product for diagnosing, preventing, or treating the disease or condition. A potential alternative product may be considered “unavailable” if there are insufficient supplies of the approved alternative to fully meet the emergency need.

A potential alternative product may be considered "inadequate":

- if, for example, there are contraindicating data for special circumstances or populations (e.g., children, immunocompromised individuals, or individuals with a drug allergy),
- if a dosage form of an approved product is inappropriate for use in a special population (e.g., a tablet for individuals who cannot swallow pills).

4. PRE-SUBMISSION

Early engagement between an applicant and SFDA about potential emergency use authorization products will facilitate more complete requests and enhance the ability to review and grant the authorization as appropriate.

SFDA strongly encourages the applicant of a product that might be considered for an emergency use authorization, particularly one at an advanced stage of development, to contact the Drug Sector before submitting a formal request.

Pre-submission activities are not a substitute for applicant efforts to develop the product toward approval, including submission and, when appropriate, implementation of proposals for clinical trials designed to determine whether the product is safe and effective for its intended use.

5. REQUEST FOR EMERGENCY USE AUTHORIZATION

5.1. Information Recommendation

1. Summary of Recommended Information and/or Data

SFDA recommends that a request for an authorization include a well-organized summary of the available scientific evidence regarding the product's safety and effectiveness, risks (including an adverse event profile) and benefits, and any available, approved alternatives to the product. The exact type and amount of data needed to support an emergency use authorization may vary depending on threat of emergency and the nature of the candidate product. SFDA may seek additional data and information on a case-by-case basis to ensure that the criteria for issuance of an authorization are met.

The following information should be submitted in any request:

- A description of the product and its intended use (e.g., identification of the serious or life-threatening disease or condition for which the product may be effective; where, when, and how the product is anticipated to be used; and/or the population(s) for which the product may be used);
- A description of the product's regulatory status:
 - whether the product is unapproved by SFDA or whether it is approved but the authorization is for an unapproved use);
 - whether the product is approved by other regulatory agencies for either the proposed use or another use;
 - clarify whether product or intended use is under an investigational application
 - information on the use of the medicinal product by either another regulatory agency or an international organization (e.g., the World Health Organization (WHO));



- The need for the product, including identification of any approved alternative product(s) and their availability and adequacy for the proposed use, and the unmet need(s) the emergency use authorization would address;
- Available safety and effectiveness information for the product (discussed in more detail below);
- Information on chemistry (as applicable), manufacturing, and controls; a list of each site where the product, if authorized, is or would be manufactured, and the current CGMP status of the manufacturing site(s);
- Information about the quantity of finished product on hand and the capabilities of the manufacturing site(s);
- Information comparable to the Summary of the product characteristics (SPC) and patient information leaflet (PIL);

2. Recommended Safety Information

i. General

The amount and type(s) of safety information recommended to be submitted as part of a request for an emergency use authorization will differ depending upon a number of factors, including whether the product is approved for another indication and, in the case of an unapproved product, the product's stage of development. For some medicinal products, data from controlled clinical trials will be available. For others, it is expected to consider clinical experience from other than a controlled trial if the circumstances warrant. Safety information is mainly interpreted in light of the seriousness of the clinical condition, prophylaxis, or alternative therapies (if any), and the specific circumstances of the emergency or threat of emergency.

ii. Unapproved Uses of Approved Medicinal Products

If the new indication uses a similar dose, duration, route of administration, or mechanism of action, and the intended patient population is similar, to that for which the product is approved, SFDA recommends that the request for an emergency use authorization reference the approved product's application. If the new use poses a different risk to the

patient population (e.g., suggesting the possibility of increased toxicity), SFDA recommends that information from relevant in vitro studies, animal toxicology studies, and (if available) human clinical data and experience be provided to support such a use.

iii. For Unapproved Medicinal Products

SFDA recommends that any request for consideration for an emergency use authorization includes the following:

- Available preclinical testing data, such as in vitro and animal toxicology data.
- Human safety information from clinical trials and individual patient experience, if available.
- When animal data are used, sufficient information should be provided to link the results of these data to expected exposures to the medicinal products related to the proposed use in humans.
- Any information on safety associated with use in humans of this or related compounds of a similar design.

iv. Risk Management Plan (RMP)

If providing a stand-alone Risk Management Plan (RMP) is not feasible. At the minimum, the information outline below should be described:

- Based on the discussion of the available safety information, a summary of the *important identified risks, important potential risks, and missing information* of the medicinal product should be addressed (definitions are illustrated in the Saudi good pharmacovigilance practices guideline (GVP)).
- The applicant should provide pharmacovigilance plan that describes the routine and additional pharmacovigilance activities and action plan for each safety concern. Studies in the pharmacovigilance plan should relate to the safety concerns identified in the safety Specification whether the studies are intended to identify and characterize risks, or to assess the effectiveness of risk minimization activities.



- The applicant should describe the risk minimization measures that will be taken to mitigate each addressed risk. They may consist of routine risk minimization (e.g. labeling the risk in the SPC or PIL) or additional risk minimization measures (e.g. educational prescriber guide or patient alert card).
- If a patients' or healthcare providers' educational material are proposed by the applicant as an additional risk minimization measure, a draft should be provided with the emergency use authorization application. Local regulations regarding additional risk minimization measure should be taken into consideration and an Arabic version of patients' educational material should be provided.
- All medicinal products granting emergency use authorization are required to distribute a *Direct healthcare-professional communication (DHPC)*, a letter which will be drafted by the applicant and approved by the SFDA; aiming to inform healthcare providers about the following:
 - That SFDA has authorized the emergency use of the product (including the product name and an explanation of its intended use).
 - the significant known and potential benefits and risks of the emergency use of the product, and the extent to which such benefits and risks are unknown.
 - The letter should be accompanied by the "Fact Sheet" (described within this guidance under section 7. Conditions of Authorization).

Important note: This is the only part that the health entities (hospitals) and government sponsors is requested to submit.

3. Recommended Effectiveness Information

It is recognized that comprehensive effectiveness data are unlikely to be available for every emergency use authorization candidate product, and the information necessary to authorize emergency use of a product will also depend on the circumstances of the emergency, as well as available knowledge about the product's safety profile. SFDA plans to assess the sufficiency of the effectiveness data and the risk-benefit profile of each candidate product on a case-by-case basis.



SFDA recommends that requests for consideration for emergency use authorizations include any available relevant scientific evidence regarding the following:

- Product's mechanism(s) of action to diagnose, treat, or prevent the disease or condition underlying the request;
- Preclinical testing data, such as in vitro evidence of the effect of the product in preventing or reducing the toxicity of the specified agent;
- Data on activity or effectiveness in animals that would contribute to understanding potential effects in humans, including but not limited to any animal efficacy studies available for products being developed;
- Evidence from human experience relevant to assessing activity, effectiveness, and dosing (e.g., in published case reports, uncontrolled trials, controlled trials, and any other relevant human use experience);
- Data to support the proposed dosage for the intended use (including pharmacokinetics and pharmacodynamics data, and for vaccines or antibody therapies, immunogenicity and/or achievement of protective levels of relevant parameters of immunity);

4. Other Data Considerations

SFDA recommends that a request for an authorization include the following types of data, as appropriate and to the extent feasible:

- Well-organized study reports that provide a complete assessment and analysis, including any statistical analyses, of available safety and effectiveness data and an interpretation of the findings. If final study reports are not yet available, any available interim study reports should be provided and clearly identified as such; and
- Source data for clinical studies, nonclinical laboratory studies, and any animal studies that contribute to assessing activity or effectiveness of the product in the treatment of the underlying disease or condition or a closely related disease or

condition, such as case report tabulations for key studies; case report forms for all patients who died during the clinical studies and for all persons who did not complete the study due to an adverse event, regardless of causality; relevant reports in the published literature; and translations of source materials that are in a language other than English.

It is recommended that requests for emergency use authorization include statements on whether the nonclinical laboratory studies were conducted in compliance with applicable Good Laboratory Practice for Nonclinical Laboratory Studies regulations (GLP) and whether the clinical studies were conducted in compliance with applicable Good Clinical Practice standards. Also specifying the methods and quality systems used to ensure the quality and integrity of data from any animal studies submitted in support of an emergency use authorization request but not performed under GLP.

Data from any ongoing testing (e.g., longer term stability data) or other data or information that may change SFDA's evaluation of the product's safety or effectiveness and that become available during the period of review or the term of the emergency use authorization. Such data should be submitted when such data become available, including any appropriately controlled clinical trials conducted in parallel with the emergency use authorization during the emergency response.

5. Discussion of Risks and Benefits

SFDA recommends that a request for an authorization include a discussion of the candidate product's known and potential risks and benefits, which includes a synthesis of the data and information requested above, including:

- Limitations, uncertainty, and data gaps;
- A description of circumstances, if any, under which the product should not be used (e.g., contraindications); and
- To the extent known, information concerning the threats posed by the candidate product (actually or potentially) involved, and anticipated response and operational considerations that may be relevant to an assessment of risks and benefits.



5.2. Format of submission

Submissions, including cover letter, may be provided in electronic or paper format. They should be briefly describing the content and organization of the included materials.

SFDA expects material to be provided in a reviewable form and sufficiently complete to permit substantive review. It is recognized during unexpected emergency circumstances it may not be possible for an applicant to provide all of the requested data or to provide it in the format suggested in timely manner. Therefore, SFDA will accept and evaluate the request based on data in the form the sponsor is able to submit. However, a request that is missing data, poorly documented, or otherwise incomplete will make the determination of whether the product's benefits outweigh its risks more difficult and could result in a request for additional information, the need for a longer time period for review, or a decision not to authorize emergency use of the candidate product.

The electronic request -as explained above- should be sent to the following email address:

- ❖ Special email address will be initiated for this procedure.

6. PROCESSING THE REQUEST

SFDA is prepared to issue the authorization expeditiously and the timelines for review and action on a request will be determined on a case-by-case basis and will depend on factors such as:

- The product profile;
- The existence, if any, of pending applications for the product;
- The nature of the emergency, potential emergency, or threat of emergency;
- Completeness of the request submission.

An authorized request will consist of (1) the signed letter of authorization and (2) any accompanying authorized materials, when necessary.

7. CONDITIONS OF AUTHORIZATION

SFDA may establish conditions on an emergency use authorization necessary or appropriate to protect the public health as following:

1. Information Relating to the Authorized Product

a. Information for Health Care Professionals or Authorized Dispensers

For an unapproved medicinal product and for an unapproved use of an approved product SFDA must establish conditions to ensure that health care professionals who administer the product are informed:

- That SFDA has authorized the emergency use of the product (including the product name and an explanation of its intended use);
- Of the significant known and potential benefits and risks of the emergency use of the product, and the extent to which such benefits and risks are unknown; and

Therefore, SFDA recommends that a request for an emergency use authorization include a "Fact Sheet" for health care professionals or authorized dispensers that includes essential information about the product. In addition to the required information, Fact Sheets should include:

- A description of the disease/condition;
- Any contraindications or warnings;
- Dosing information (if applicable), including any specific instructions for special populations; and

Contact information for reporting adverse events and additional information about the product.



b. Information for patients:

SFDA recommends that a request for an emergency use authorization include a “summary information” for patients that includes essential information about the product as following:

- The SFDA has authorized emergency use of the product;
- Product name and explanation of the intended use of the product;
- A description of the disease/condition
- Significant known and potential benefits and risks associated with the emergency use of the product, and of the extent to which such benefits and risks are unknown;
- That they have the option to accept or refuse the emergency use authorization product and of any consequences of refusing administration of the product; and
- ADE reporting methods

2. Monitoring and Reporting of Adverse Events

Any detected adverse drug events should be submitted to the SFDA through the ICSR reporting channels as illustrated in the Saudi good pharmacovigilance practices guideline.

3. Submission of periodic safety update reports:

For an unapproved use of an approved product, the request should include the updated periodic safety update report for the product according to the PSUR submission requirements that were addressed in the Saudi good pharmacovigilance practices guideline.

8. TERMINATION OF AN AUTHORIZED PRODUCT

Emergency use authorization is terminated for certain product or indication when the MOH declared that the circumstances that precipitated the authorization have ceased or a change in the approval status of the product such that the authorized use(s) of the product are no longer unapproved. For example, an authorization issued to allow an unapproved use of an approved product may no longer be needed if that product is later approved by SFDA for the use permitted by the emergency use authorization.



REFERENCE

- FDA Emergency Use Authorization of Medical Products and Related Authorities (Guidance for industry and other stakeholders), January 2017.