الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Conditional Approval for Medicinal Products for Human Use

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Version 1

Saudi Food & Drug Authority

Drug Sector

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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

Document Control

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1. INTRODUCTION

The Saudi Food and Drug Authority (SFDA) supports the development of new medicines to address the unmet medical need in the treatment of a serious or life threatening condition. In order to meet unmet medical needs of patients and in the interests of public health, it may be necessary to grant marketing authorizations on the basis of less complete data than is normally the case and subject to specific obligations, hereinafter 'conditional approval'.

Conditional approval is issued for products determined by SFDA when technical requirements that must be provided in the dossier are not met or completed and the benefits of the product outweigh its potential risks. SFDA has adopted this accelerated pathway to facilitate timely access of promising new therapies while ensuring the scientific rigor of the assessment of their quality, safety, and efficacy. However, conditionally approved medicinal products are exclusively for government health sector supply.

1.1. Scope

This document lays down rules on the granting of Conditional Approval for new human medicines, including biologics, subject to specific obligations in accordance with SFDA's requirements.

1.2. Legal basis

The legal basis for the conditional approval is Chapter 3, Article 18 of the Registration Rules of Pharmaceutical, Herbal, and Health Product Manufacturers and their products Guideline.

1.3. Related documents

This document should be read in conjunction with the following drug sector documents:

- Regulatory Framework for Drugs Approval.
- Guidance for Submission.
- Data Requirements for Human Drugs Submission.
- GCC Module 1 Specifications.
- Guideline on Good Pharmacovigilance Practices (GVP).
- The GCC Guidance for Presenting the Labeling Information, SPC and PIL.

2. GRANTING OF A CONDITIONAL APPROVAL

2.1. Eligibility Criteria

This document shall apply to new medicinal products, including biologics, for human use and belong to one of the following categories:

1. Medicinal products which aim at the treatment, the prevention or the medical diagnosis of seriously debilitating diseases or life-threatening diseases;

   The severity of the disease, i.e., its seriously debilitating, or life-threatening nature needs to be justified, based on objective and quantifiable medical or epidemiologic information. Whereas a life-threatening disease is relatively easy to describe based on figures of mortality and life expectancy, justifying that a disease is seriously debilitating will have to consider morbidity and its consequences on patients' day-to-day functioning. For a disease to be considered seriously debilitating it would need to have a well-established major impact on patients' day-to-day functioning either already early in the course of the disease, or in the later stages. These aspects should be quantified in objective terms, as far as possible.

2. Medicinal products to be used in emergency situations; such as in the situation of a pandemic; in response to public health threats duly recognized either by the World Health Organization or by the Ministry of Health of Saudi Arabia.

2.2. Requirements

A conditional approval may be granted where SFDA finds that, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, all of the following requirements are met:

a) The risk-benefit balance of the medicinal product is positive

For the demonstration of a positive benefit-risk balance, the available evidence should be sufficient to demonstrate the benefits of the medicinal product to a degree that allows them to be assessed against the risks identified in the studies conducted and the risks related to the absence of some of the data. A comprehensive non-clinical and pharmaceutical data should be available and only the

clinical data could be less comprehensive than is normally the case. Occasionally, SFDA may, in its discretion, accept incomplete preclinical or pharmaceutical data, such–applications will be assessed on a case-by-case basis.

The data that are not available at the time of application and authorization should be discussed by the applicant, and the acceptability of less comprehensive data justified, based on the strength of available results, and taking into account the requirement for a positive benefit-risk balance. The establishment of beneficial effects at the time of authorization could potentially be based on endpoints that are fully validated surrogate endpoints and reasonably likely to translate into clinical benefit, but do not directly measure the clinical benefit.

The safety profile of the medicinal product should be adequately defined and appropriate to justify a positive benefit-risk balance. The acceptability of safety of the medicinal product must be assessed on a case-by-case basis, based on the available safety data and taking into account the demonstrated benefits of the medicinal product.

b) It is likely that the applicant will be in a position to provide the comprehensive clinical data

By way of specific obligations, the holder of a conditional approval shall be required to complete ongoing studies or to conduct new studies, with a view to provide comprehensive clinical data confirming that the benefit-risk balance is positive. The applicant should explain how comprehensive data can be provided within an agreed timeframe.

The applicant is strongly encouraged to discuss in advance of the submission of an application the overall development plan and design of studies that, on one hand, are planned to be completed before authorization and, on the other hand, will be conducted as specific obligations following the granting of a conditional approval.

c) Unmet medical needs will be fulfilled

The unmet medical needs mean a condition for which there exists no satisfactory method of diagnosis, prevention or treatment or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected.

To address this requirement, applicants should justify that there exists an unmet medical need and

that it is necessary to introduce new methods when no satisfactory methods exist, or that it is necessary to provide a major improvement over the existing methods. The demonstration of fulfilment of an unmet medical need has to be justified on a case-by-case basis. The justifications should quantify the unmet medical need based on medical or epidemiologic data.

In general, major therapeutic advantage would normally be based on meaningful improvement of efficacy or clinical safety. The advantages should be demonstrated over existing methods used in clinical practice (if any), using robust evidence, normally from well conducted randomized controlled trials (evidence-based demonstration of benefit).

In order to support the claim that unmet medical needs will be fulfilled, the applicant shall provide:

- A critical review of available methods of prevention, medical diagnosis or treatment, highlighting an unmet medical need.
- Quantification of the unmet medical need taking into account technical argumentation (e.g., quantifiable medical or epidemiologic data).
- A justification of the extent to which the medicinal product will address the unmet medical need.

d) The benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required

The applicant will have to provide a justification to substantiate the claim that the benefits to public health of the immediate availability of the medicinal product outweigh the risks inherent in the fact that additional data are still required. The justification should assess the impact of immediate availability on public health, based as far as possible on objective and quantifiable epidemiological information, as opposed to availability when comprehensive clinical data are expected to be available. Similarly, the risks inherent in the fact that additional data are still required shall be quantified as far as possible on objective and quantifiable terms.

In order to support the claim that the benefits to public health outweigh the risks inherent in the fact that additional data are still required, the applicant will have to provide a justification addressing the following points:

- Benefits to public health of the immediate availability on the market of the medicinal product.
- Risks inherent in the fact that additional data are still required.
- How the benefits to public health in the context of immediate availability outweigh the risks.

2.3. Product Information:

Enhanced transparency regarding the assessment of such applications and clear information should be provided to patients and healthcare professionals on the conditional nature of the authorizations. Add the inverted equilateral black triangle symbol and the explanatory statement at the top of the summary of product characteristics and the package leaflet for medicinal products subject to additional monitoring (refer to *the GCC Guidance for Presenting the Labeling Information, SPC and PIL*).

2.4. Post-approval Obligations

Given the intent to speed up regulatory approval processes for new therapies, the holder of conditional approval shall be required to provide further data from ongoing studies or to conduct new studies within specified deadlines in order to clarify any outstanding questions on quality, safety and efficacy to confirm that the benefits continue to outweigh the risks. In addition, specific obligations may be imposed in relation to the collection of pharmacovigilance data and an updated risk management plan file in accordance with *Saudi Good Pharmacovigilance Practice Guideline*. The time schedule for submitting periodic safety update reports (PSUR) should be adapted to accommodate the validity of the conditional approval.

The company should submit the summary monthly report after getting the approval from SFDA for 6 months and should include as a minimum:

- Interval / cumulative exposure of product in Saudi Arabia and worldwide
- Interval / cumulative number of serious and non-serious case reports, overall and by age groups and in special populations (e.g. pregnant women)
- Actions taken by regulatory agencies for safety reasons
- Changes to reference safety information
- New, ongoing and closed signals with signal evaluation
- Causality assessment evaluation of serious adverse events, including fatal cases
- Summary of efficacy and safety findings from clinical studies (completed or ongoing)
- Benefit-risk evaluation

However, SFDA can also take regulatory action if the company failed to comply with the imposed obligations for conditional approval.

3. APPLICATION FOR CONDITIONAL APPROVAL

3.1. SFDA Advice Prior to Conditional Approval Application

Applicants for a potential conditional approval may request SFDA advice, as applicable, on whether a specific medicinal product being developed for a specific therapeutic indication falls within one of the categories set out in section 2.1, and fulfils the requirements. However, the intention to request conditional approval and any practical or procedural issues with regard to a potential request for conditional approval should be addressed at pre-submission meetings with SFDA.

The applicants are reminded that prospective planning of conditional approval is important for avoiding delays in assessment procedure, and is especially important in cases when rolling review is undertaken. As medicinal products addressing unmet medicinal needs are expected to be of major interest from the point of view of public health, applicants are encouraged to duly consider the appropriateness of seeking rolling submission for medicinal products suitable for a conditional approval. On a case-by-case basis, SFDA may accept rolling submissions during the evaluation phase, where this information might have an impact on the registration decision (see *Guidance for Submission*).

3.2. Application Process

Step 1: Requesting conditional approval

- A formal request for conditional approval must be presented by the applicant through SDR.drug@sfda.gov.sa, accompanied by details showing that the product falls within the scope of the eligibility criteria and satisfies the requirements.
- Applicants are advised to organize a pre-submission meeting with SFDA to discuss planned applications for conditional approval.

Step 2: SFDA response

- SFDA evaluates the eligibility request and supporting documentation, and then provides the applicant with SFDA's opinion via e-mail on whether the request is accepted or not.

Step 3: Application

- As the request is accepted, the applicants should submit the application via the Saudi Drug Registration (SDR) System using the electronic common technical document (eCTD) format.
- If it is not possible to comply with the eCTD format submission, applicants can request an exception through SDR.drug@sfda.gov.sa
    - Although such submissions will be exempted from filing in eCTD format, all documents should be provided in an electronic form only, and SFDA encourages applicants to follow the CTD structure.

Step 4: Notification of application

- The applicant must notify SFDA of the submission immediately via e-mail to allocate the required resources.

Step 5: Assessment of the application

- This step is the same as for the regular review process, although the clinical data provided as part of a submission for conditional approval may be preliminary, this does not mean that the evaluation workload would be less than for a standard submission for registration.
- SFDA will take into consideration the standard timetable agreed for the assessment procedure.

Step 6: Decision

- SFDA issues the decision as to whether conditionally approve the product. The decision to grant conditional approval will be provided to the applicant with a conditional approval letter.
- The decision to approve is always made by SFDA on the basis that the benefits outweigh the risks.
- Applicants must fulfill specific post-approval obligations within predefined timelines.

Note: SFDA has the authority to grant Conditional Approval for applications under another registration pathway to facilitate timely access to certain eligible medicines.

4. LAPSING OF CONDITIONAL APPROVAL

The conditional approval is effective for two years, and this approval is not intended to remain conditional indefinitely. Upon review of information collected during the conditional approval period, a drug could be:

- Withdrawn if new data show that the product's benefits no longer outweigh its risks. SFDA can also take regulatory action, such as suspending or revoking the approval if the applicant fails to fulfil post approval obligations;
- Transition to full registration once the company fulfil the obligations imposed and the complete data confirm that the product's benefits continue to outweigh its risks; or
- Application for an extension to the conditional approval period.

4.1. Extension of Conditional Approval

Up to two extensions, each of 2 years are available, resulting in a possible maximum conditional approval period of 6 years. The marketing authorization holder shall apply for its extension at least 6 months before the conditional approval is due to end, and shall provide SFDA with a report on the fulfilment of the specific obligations to which it is subject.

The extension application will be assessed on the basis of the benefit-risk balance and formulate an opinion whether the specific obligations or their timeframes need to be retained or modified and whether the marketing authorization should be maintained, varied, suspended or withdrawn.

4.2. Transition to full registration

When submitting the last specific obligation data and in view of a possible change to a standard marketing authorization, the marketing authorization holder should address this in their submission and provide updated product information and a clinical expert statement in support of the possible granting of a standard marketing authorization. Once the specific obligations are fulfilled and the marketing authorization is issued, the marketing authorization will be valid for 5 years.