الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Guidance for Orphan Drug Designation

Draft

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This document is a draft SFDA guideline published for comments and suggestions purposes. It is, therefore, subject to alteration and modification and may not be referred to as SFDA guideline until approved by SFDA

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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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Draft	Executive Directorate of Regulatory affairs	29 August 2022	-

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Glossary

Orphan Drug	A drug designated as such according to this guidance and intended for orphan indication in a rare disease or condition
Orphan Indication	The proposed indication submitted by the applicant for the purpose of orphan designation for a drug to diagnose, prevent or treat a life-threatening or seriously debilitating condition or disease
Orphan Drug Designation (ODD):	Process of validation and verification of orphan-drug status to establish eligibility of drugs for the benefits and incentives of development of orphan drugs provided by the SFDA.
Sponsor	Any legal or natural person, established in Saudi Arabia, seeking to obtain or having obtained the designation of a drug as an orphan drug. It is the entity responsible for a clinical or nonclinical investigation of a drug, including the responsibility for compliance with applicable provisions of the act and regulations.
Incentives	Measures provided by SFDA to support and encourage the manufacturing and research and development activities of designated orphan drugs.

1. INTRODUCTION

The Drug Sector in the Saudi Food & Drug Authority (SFDA) has developed this guidance to provide information to the sponsor on how to submit an application to designate the orphan drug

It is important to note that the SFDA reserves the right to request information or defined conditions not specifically described in this document, in order to allow the administration to adequately assess the safety, efficacy and quality of medicinal products.

This guidance should be read in conjunction with the other relevant and applicable guidance documents.

1.1. Scope

This guidance document provides information to sponsors who are intended to apply for orphan drug designation (ODD) at any stage of the development of the human medicinal product and before submitting the marketing authorization holder.

1.2. Objectives

To establish eligibility of drugs for the benefits and incentives granted by SFDA to orphan drugs after obtaining orphan drug designations.

2. ORPHAN DRUG DESIGNATION

SFDA reviews ODD applications to develop and/or market drugs for orphan indication in rare diseases, known as “orphan drugs”. Designated orphan drugs can apply for certain measures and incentives to support the research and development, registration and marketing activities.

3. ORPHAN INDICATION ELIGIBILITY CRITERIA

3.1. One indication

The sponsor should submit one ODD application for only one orphan indication per drug or one orphan indication per dosage form with considerations of intellectual property.

If the sponsor seeks ODD for more than one indication, separate designation applications need to be submitted for each orphan indication. In this regard, ‘treatment’ and ‘prevention’ or ’diagnosis’ of the same condition are considered separate indications and should be the subject of separate applications for designation.

The potential orphan drug must be:

- An unregistered drug in SFDA, or
- An already registered drug in SFDA with
    - a new orphan indication, or
    - a new dosage form, or
    - other major variation applications that meet all relevant criteria of ODD

3.2. Seriously debilitating diseases or life-threatening conditions or diseases

(a) The term "life-threatening" means:

(1) Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted; and

(2) Diseases or conditions with potentially fatal outcomes, where the endpoint of clinical trial analysis is survival.

(b) The term "severely debilitating" means diseases or conditions that cause major irreversible morbidity.

Orphan drug product should be intended for the diagnosis, prevention or treatment of a life-threatening or seriously debilitating condition or disease. Defining a particulary serious disease or condition should be in terms of their specific characteristics, e.g. pathophysiological, histopathological, clinical characteristics. It is also considerable with

a medical plausibility justification if the condition is a subset of a distinct medical entity and has a plausible link to the condition but the drug cannot exert pharmacodynamics effects beyond the subset. In addition, the sponsor should provide a valid rationale for the use of the drug in the proposed orphan indication.

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. Furthermore, serious debilitation, or fatal outcome should be a prominent feature of the target disease and therapeutic indication, i.e. affect an important portion of the target population.

3.3.Prevalence of rare disease or condition OR lack of financial viability

Any life-threatening, seriously debilitating or serious and chronic condition which

(A) Affects fewer than 5 in 10,000 individuals in Saudi Arabia when the application is made, Prevalence disease or condition should represent the number of patients in Saudi Arabia who have been diagnosed as having the disease or condition at the time of the submission of the ODD application.

OR

Any life-threatening, seriously debilitating or serious and chronic condition which

(B) affects more than 5 in 10,000 individuals in Saudi Arabia but for which there is no reasonable expectation that the cost of developing and making available in Saudi Arabia a drug for such disease or condition will be recovered from sales of such drug (lack of financial viability).

3.4. Under development for this orphan condition

Sponsors can apply for orphan designation at an early or late stages in drug development before submitting the application for marketing authorization.

3.5. Comparison with other methods for diagnosis, prevention or treatment of the condition

- **Justification as to why methods are not satisfactory:** the sponsor should provide justification as to why the methods reviewed are not considered satisfactory. This may be based on either clinical information or on scientific literature. It should be noted that where drugs authorized in the proposed orphan indication exist they would be viewed as 'satisfactory methods' and the sponsor would be required to argue 'significant benefit'. If this section is completed, it is not necessary to complete section D3 of the ODD application template regarding justification of significant benefit and vice versa. Or

- **Justification of significant benefit:** alternatively, and in particular where there already exist authorized drugs, the sponsor should provide justification for the assumption that the drug for which designation is sought will be of significant benefit to those affected by the condition. This justification should make reference to appropriate scientific literature or the results of comparative studies, whether of a definitive or preliminary nature. If this section is completed, it is not necessary to complete section D2 of the ODD application template regarding justification as to why methods are not considered satisfactory and vice versa.

4. INCENTIVES OF ORPHAN DRUG DESIGNATION

Orphan designation qualifies the sponsor of the drug for various registration and development incentives provided by SFDA. Incentives of orphan drug designation may

include a collection of measures to support and encourage the registration and research and development activities for designated orphan drugs.

The sponsor or marketing authorization holder (MAH) can request the list of incentives needed from the SFDA after granting an orphan drug designation, and ordered by priority in the application of orphan drug designation. After reviewing the orphan drug designation application, the SFDA reserves the right to designate the possible incentives that can be granted to the designated orphan drug. The list of incentives of orphan drug designation include:

- Pre-submission meetings
- Priority review
- Scientific & regulatory advice and consultation provided by the Drug sector.
- Marketing Exclusivity (according to SFDA Regulation of Marketing Exclusivity Guidance)
- Pricing (according to SFDA Rules of Pricing of Pharmaceutical Products Guidance)

5. TIMING OF SUBMISSIONS

A sponsor applying for the designation of a new product as an orphan drug can apply for designation at any stage of the development before submitting the application for marketing authorization.

6. ORPHAN DESIGNATION PROCEDURE

1. Sponsor submits a request to notify SFDA of intent to submit orphan drug designation application through Sdr.drug@sfda.gov.sa
2. Pre-submission SFDA meeting with sponsor
3. Submission of orphan drug designation (ODD) application by sponsor
4. Application validation by SFDA
5. Assessment and recommendations for orphan drug designation
6. Final decision to be adopted
7. Publication of public summary of ODD on SFDA website

7. POST DESIGNATION

- A post-designation report on the state of development of designated drugs needed to be submitted annually to maintain the orphan drug designation.
- Requests of amendment, withdrawal or transfer of orphan-drug designation, enclosed with the documents and details, need to be approved first by the SFDA to keep maintaining the ODD.
- SFDA may revoke, suspend or withdraw orphan-drug designation for any drug if the SFDA finds that drug had not been eligible for orphan-drug designation at the time of submission of the application.

8. ELECTRONIC SUBMISSION OF ODD APPLICATION

- The SFDA accept electronic-only applications for ODD, applicants should submit their applications as a CD or DVD with a signed cover letter and use the Application for orphan drugs designation templet.
- If more than one indication is applied for the same product, separate applications should be submitted for each orphan indication.
- In this regard, 'treatment' and 'prevention' of the same condition are considered as two separate indications and should be the subject of two separate applications for orphan designation.

For any questions please e-mail Sdr.drug@sfda.gov.sa

ANNEX

Application for orphan drug designation

Sections A to E (scientific part)

The purpose of this template is to facilitate sponsors in completing the scientific part (sections A-E) of the application for orphan designation.

Please fill in the template without amending the styles and the format. Please do not use hyperlinks.

<Date>

Reference number	<Text>
Active substance[s]:	<Text>
Orphan indication	<Text>

Table of contents

List of abbreviations

An abbreviations list must be provided with each application.

<Text>

Sections A-E

A. Description of the condition

A1. Details of the condition

<Text>

Definition

<Text>

Aetiology

<Text>

Specific characteristics; pathophysiological, histopathological, clinical characteristics

<Text>

Classification

<Text>

Diagnosis and symptoms

<Text>

A2. Proposed orphan indication

<Text>

A3. Medical plausibility

A.3.1. Active substance: description of the drug, pharmacological class and mode of action

<Text>

A.3.2. Plausibility of the orphan condition; data with the specific product as applied for designation in specific models or in patients affected the condition

<Text>

A4. Justification of the life-threatening or debilitating nature of the condition

<Text>

B. Prevalence of the condition

B1. Prevalence of the orphan disease or condition in the Saudi Arabia

<Text>

B2. Prevalence and incidence of the condition in the Saudi Arabia

<Text>

C. Potential for return on investment

<Text> *or* Not applicable. *(delete C1-C5 if not applicable)*

C1. Grants and tax incentives

C2. Past and future costs

C3. Production and marketing costs

C4. Expected revenues

C5. Certification by registered accountant

D. Other methods for diagnosis, prevention or treatment of the condition

D1. Details of any existing diagnosis, prevention or treatment methods

<Text>

D2. Justification as to why methods are not satisfactory

<Text> *or* Not applicable. *(delete as appropriate)*

Note that sections D2 and D3 are mutually exclusive.

D3. Justification of significant benefit

<Text> *or* Not applicable. *(delete as appropriate)*

E. Description of the stage of development

E1. Summary of the development of the product

<Text>

Quality aspects

Non-clinical aspects

Proof-of concept in relevant model

Pharmacology

Pharmacokinetics

Toxicology

Clinical aspects

Pharmacokinetics

Pharmacodynamics

Clinical efficacy

Dose-response studies and main clinical studies

Clinical studies in applied condition

Planned clinical studies

Clinical safety

Adverse events

Serious adverse events and deaths

E2. Details of current regulatory status and marketing history in the Saudi Arabia and other countries

Sponsor's position:

An application for marketing authorisation has previously been submitted to the SFDA for this drug, with the proposed invented name of <(tradename)>, in <indication>. The application was withdrawn in <year>.

This drug product is currently authorised by the SFDA, with the invented name of <(tradename)>, for the following indication(s): <indication>

This drug was not authorised in the Saudi Arabia and other countries at the time of submission of the application.

Scientific advice or protocol assistance on this drug was given by the SFDA in <month/year>.

In the US, orphan drug status was granted on <date> for <indication>.

In the EMA, orphan drug status was granted on <date> for <indication>.

In the <county>, orphan drug status was granted on <date> for <indication>.

Please delete any paragraph above that does not apply.

F. Bibliography

This section should contain all published references referred to in section A to D above and should be submitted together with the application. Where information is printed out from a web-site the date that the web-site has been accessed should be noted.

The preferred format for cross-referencing published literature in Section A-E of the application is by the lead author and year e.g. (Smith et al, 2002). Please do not use hyperlinks.

<Text>