Ethiopian Food and Drug Authority (EFDA)

Guideline for Registration of Oral Care and Skin Care Products with Therapeutic Claims

1st edition

July 2020

Addis Ababa

Contents

Abbreviation

ADE	Adverse Drug Event
EFDA	Ethiopian Food and Drug Authority
GMP	Good Manufacturing Practice
MA	Marketing Authorization
PPM	Part Per million
SPF	Sun Protection Factor
UV	Ultraviolet
UVA	Ultraviolet A
UVB	Ultraviolet B

1 Background

The Ethiopian Food and Drug Authority (EFDA) is mandated by the proclamation No. 1112/2019 to ensure the safety, efficacy and quality as well as rational use of medicines. Article19(1) of the proclamation decrees that "the rigor of regulatory assessment of medicines and medical devices shall be commensurate with the products type, nature and potential risk to human health". The evaluation process to ensure safety, efficacy and quality of skin care and oral care products with therapeutic claim, which are preventive in nature, needs a relatively minimum exertion to ease the accessibility of the products for consumers use. Marketing authorization applications for skin care and oral care products with therapeutic claim are one of the category of pharmaceuticals that fall in the jurisdiction that permits shortened assessment as they are generally considered as the least risky therapeutic products that needs marketing authorization for marketing in Ethiopia.

One of the EFDA`s current strategic directions is to risk categorize products for risk-based dossier assessment and expedite marketing authorization processes. Accordingly, this sub group of low risk products are designated discretely as the implementation of the strategy requires further classification of low risk products in to different classes so as to further risk proportionate marketing authorization applications. For oral care and skin care products with therapeutic claim, the evaluation process will be limited to a brief review of available data and information; focusing on the assessment of administrative requirements, labelling information & specifications, stability and shelf life, and other technical data as applicable. Review of administrative documents and selected technical requirements based on national or international standards as well as compliance with cGMP as applicable are the major requirements for the marketing authorization of these products.

The intention of this guideline is to set criteria for applications to be submitted for granting marketing authorization for oral care and skin care products with therapeutic claim.

All users of this guideline are kindly requested to forward their valuable comments and suggestions to the Food and Drug Control Authority of Ethiopia, via P.O. Box 5681, Tel. 251-11 552 41 22, or email: regulatory@fmhaca.gov.et, Addis Ababa, Ethiopia.

2 Definition

For the purpose of this guideline the following definitions are applicable.

Low risk product means a medicinal product that contain known chemical entity with established safety profile over years, indicated for well documented conditions, provided by conventional dosage forms such as oral solids, liquids, and topical preparations.

Oral care products means products that contain therapeutic agents designed to control various diseases and conditions of the mouth such as dental decay, gum diseases, plaque and tooth sensitivity as well as different interdental cleansers and accessories that are primarily designed for the mechanical removal of plaque. These include but not limited to tooth paste based with fluoride content of 1500ppm or above (ordinary tooth paste, Herb tooth paste & functional tooth paste), tooth powder, tooth whitening gel, mouth wash and dentifrices.

Skin care products means products applied for a range of practices that support skin integrity, enhance its appearance and relieve skin conditions. They may include products containing therapeutic claim such as “medicated” soap and products that are used for avoidance of excessive sun exposure (sunscreens). Examples of therapeutic claims include prevent aging, act as an antibacterial, protects from and treats fever blisters and cold sores, protects from and treats insect bites/stings, relieves vaginal irritation and reduce edema, restructures and repairs skin, treat boils, protect from sun and removes warts.

Sunscreen means a skin care product of any preparation type that has a Sun protection factor (SPF) of 4 and above, and intended to be placed in contact with the human skin with a view exclusively or mainly to protect from UV radiation by absorbing, scattering or reflecting radiation.

Application means an application for marketing authorization of products those are eligible for approval by oral care & skin care products with therapeutic claim application track.

3 Scope

This guideline is applicable to assessment and market authorization of all topical products designated/ listed as oral care and skin care products with therapeutic claim primarily intended for disease prevention or oral mucosal or skin protection.

Products with the primary intent for cosmetic function such as cleansing purpose (for example ordinary toothpaste, skin cleanser, hand wash etc) as well as products containing an ingredient with sun screening properties but the primary purpose of which is neither sun screening nor therapeutic should be regulated as cosmetics.

4 Objective

The main objective of this guideline is to set abridged requirements for assessment and registration of oral care and skin care products with therapeutic claim that are intended for preventive purposes so as to ease their access in the market.

5 Criteria for inclusion in the oral care & skin care products with therapeutic claim

During applying for MA of these category of products, the applicant shall give due diligence considerations to verify its suitability for marketing authorization via this approval pathway. At least the following general aspects should be considered as criteria for presumption whether a product is suitable and rational for approval by this pathway

1. Products that have therapeutic claim meant for topical application and have safe inherent characteristics (less or no possible toxicity and no skin irritation)
2. Topical products with therapeutic claim that are manufactured with less complex manufacturing process
3. Products with therapeutic claim that are basically destined for some nature of a condition being prevented (such as sun burn)
4. Products with therapeutic claim which have clear cautionary notice of the age group of the population using the product

5. Products with therapeutic claim which do not contain banned (prohibited ingredients) chemicals or beyond permissible content
6. The products primary intent is not for cosmetic function such as cleansing purpose

Accordingly, products listed in **annex I** of this guideline are generally categorized as products with therapeutic claim, based on the criteria for risk classification of products.

6 Requirements for registration of oral and skin care products with therapeutic claim

Manufacturers & importers must ensure that their products are not harmful or unsafe, and that they conform to this guideline and national or international applicable quality standards before supplying such therapeutic products for use in the country.

Applicants for MA of oral and skin care products with therapeutic claim must to full fill the following general requirements and product specific requirements.

6.1 General requirements

6.1.1 Application letter

A dated and signed letter for submission of the application by mentioning the product included in the dossier from the manufacturer and/or local agent responsible for registration, should be submitted.

6.1.2 Application form

Application form should filled and submit (as indicated in **annex II** of this guideline) to the Authority. The date of application should be consistent to the date of submission of dossier to the Authority.

6.1.3 Agency agreement

1. An agency agreement should be submitted in line with the requirements indicated under the Module 1 (Administrative and product information section) of the **Medicine registration guideline, 4th Edition,** 2020.
2. The agreement should state that if any fraud or unsuspected and unacceptable adverse event occurs to the user under normal utilization, all the party's (local agents, manufacturer, and/or license holder) mentioned in the agreement will be responsible for the product recall and for substantiating any related consequences and liable for legal action as per article 38 (4) of proclamation No 1112/2019 or other relevant laws of the country.

6.1.4 Certificate of good manufacturing practices

A copy of valid Good Manufacturing Practice (GMP) and Manufacturing License Certificate of the product manufacturer granted by the authorized body in the country of manufacture (license holder) should be provided. Generally, inspection of the manufacturing site by EFDA is not a pre-request for submission of application for registration and granting MA for these products. However, when deemed necessary, the Authority may inspect the manufacturer`s facility prior to issuance of MA or after the product has granted marketing authorization.

6.1.5 Marketing authorization status

The applicant should submit a valid marketing authorization to demonstrate that the product is registered or licensed in the country of origin. List of countries in which the product under consideration has been granted a marketing authorization and the restrictions on sale or distribution, (e.g., withdrawn from the market, etc.) along with copies of MA certificates should be provided.

6.1.6 Product information

a) Product information including list of all ingredients, the primary use or purpose of the product, effect of ingredients on the body, how the product is applied, precautionary measures and labelling should be provided
b) All product information label statements are required to be in English and/or Amharic

c) The information provided should not vary from the claims made for the same product in any other jurisdiction and any information appearing in the product information should be based on scientific justification.

d) Both immediate and outer labels should be only original labels or computer-ready colour-printed labels and in the case where the text of the labels is printed directly on primary packaging through a silk screen process, photocopies of these labels will be accepted for approval. The titles for batch number, manufacturing, and expiry dates should be part of the printing (typewritten materials, stickers, etc., are not acceptable). If the labelling technology of the manufacturer is such that this information is to be printed on the label during production, a written commitment to show all the required information on the label of the finished product must be submitted.

e) The contents of the label should at least contain:

- The name of the product– brand and/or generic
- Nature or use of the product
- Net quantity of contents of the product in the package
- Conspicuous ingredients declaration
- Indication for use
- Dosage and administration
- Appropriate label warnings and precautions
- Storage conditions
- Batch number
- Manufacturing date
- Expiry date
- Name and address of the manufacturer

6.1.7 Receipt for payment of service fees

Applicants shall pay evaluation and registration fee as per the applicable service fee regulation in force at the time of application. Each application should be accompanied by receipt of service fee paid for a specific product registration. For details, the applicants are advised to contact the Authority for the amount and modalities of payment.

6.2 Technical requirements

For registration of oral care and skin care products, applicant should provide a minimum technical information as indicated in this section of the guideline. However, when deemed necessary, the Authority may request additional information as applicable for the product under consideration.

6.2.1 Ingredients:

Preparations of oral care and skin care product with therapeutic claim should not contain ingredients from the prohibited ingredient list stated by the Authority (see annexes of cosmetic directive No. 48/2020). The manufacturer should describe ingredients including reference to each ingredient used in the preparation of the product.

6.2.2 Data on composition of the finished product

All list of ingredients which will present in the final product including the qualitative composition with their amounts on a per unit basis (including overages, if any), the function of the components, and a reference to their quality standards (e.g., compendial monographs or manufacturer's specifications) should be provided in tabular form.

The tables should be used to summarize the composition of the final product and express the quantity of each component on a per unit basis (e.g., mg per ml, mg) and percentage basis, including a statement of the total weight or measure of the dosage unit.

6.2.3 Method of manufacture of finished product

The method of manufacture should show

- Flow chart for the method of manufacture
- Concise description of the method of manufacture of the final product including the quality and quantity of the raw materials used including the final packaging and labelling procedure.

Description on the precautions and in-process controls that are made in connection with different stages of manufacturing, that is of importance in ensuring the quality of the finished product.

6.2.4 Data on specification and method of analysis of the finished product

The specification for the finished product should be provided. The specification shall describe all the relevant control parameters for the final product and their acceptance limit. The final product should at least indicate but not limited to the following information.

- Appearance (clarity, color, homoginity, odor)
- Consistency
- Particle size
- pH
- Average weight/volume
- Assay (for claimed ingredient)
- For toothpaste which contains fluoride (total fluoride, available fluoride ion, specific gravity tests)

The method of analysis of finished product should be provided. It should include test methods for all parameters indicated in the specification of the finished product. The test method should at least mention the equipment's, reagents, method etc.

The certificate of analysis of for two batches finished product which performed with the indicated method should also be submitted.

6.2.5 Container closure system of finished product

A description of the container closure systems should be provided, including the identity of materials of construction of each primary packaging component and its specification. The specifications should include description and identification (and critical dimensions, with drawings where appropriate). Non-compendial methods (with validation) should be included, where appropriate.

6.2.6 Stability Report

The real time report should be provided. The report should include the proposed shelf-life of the final product and storage conditions. The real time stability report data sheet should indicate:

a) The name of finished product
b) The batch number (minimum two) and batch type

c) Date of manufacture
d) Expiry date or any statement which may explain for example “use within two years from the date of manufacture”
e) Type and chemical nature of the packaging materials
f) Analytical methods that will qualitatively and quantitatively measure the characteristic physical, chemical and biological properties of active or functional ingredients of the finished product and distinguish them from their degradation products so that active ingredient content can be measured. If such a method is mentioned elsewhere in the dossier it is enough just to mention the page number.
g) Initial and all subsequent results of chemical, physical and/or biological testing. The frequency of testing must be every three months for the first year, every six months for the second year and every year for year thereafter.
h) Summary of the study and storage recommendations based on the data generated.

6.3 Product specific requirements

6.3.1 Requirements for Oral Care

For oral care products the label must provide the following information

1. Content of fluoride when applicable
2. Instruction for kids under 6 and fluoride contents higher than 1000µg/g
3. Cautionary notes, as applicable, such as “Not for kids under 6”; “No swallowing”; “read instruction and dilute before application”; “read instruction and mix before application” etc.

6.3.2 Requirements for skin care products

a) For “Medicated” Soaps and similar products with therapeutic claim or with antibacterial claim, the applicant must submit data demonstrating that these soaps provide additional protection from diseases and infections as compared to plain soaps. Otherwise, they must avoid wordings such as “antibacterial, medicated…. etc” on the product label and can market it as plain soaps.
b) For sunscreens, the applicant shall submit letter for declaration of absence of banned ingredients in the sunscreen. To assess the safety of ingredients used in sunscreen products

before a product is released to the market the applicant shall fulfil the testing, ingredients composition and labelling mandatory requirements. The SPF test should provide a clinical (in vivo) measurement of a sunscreen drug product's ability to protect against sunburn. The broad-spectrum test should provide an in vitro measurement of a sunscreen product's ability to protect against both UVA and UVB radiation. The label should at least indicate: -

- numerical value determined by the SPF test
- For water resistant sunscreen, provide the length of time the product is proven to be water resistant
- Warnings shall indicate do not use on broken skin, keep out of eyes, etc
- Directions for use; such as apply …. minutes before sun exposure, apply to all skin exposed to sun, limit time in the sun…etc

6.4 Application submission & assessment procedure

6.4.1 Application submission

Applications for oral care or skin care products with therapeutic claim must be submitted.

As the oral care and skin care with therapeutic claim producers applications needs the shortest review process, generally shortest MA issue target times applies to such types of applications.

Applications for registering these category of products will be validated to determine whether it is eligible for such approval pathway, complete and meets the requirements for an effective application.

The Authority may make requests for further information from the applicant if there are issues arising at any stage of the evaluation process

Granting the marketing authorization will be based on the outcome of the abbreviated review outcome.

6.4.2 The overall review process:

a) Verifying eligibility of the product under consideration

Before starting the assessment, the application needs to be verified against the list of oral care and skin care products, as indicated in **Annex I** of this guideline.

b) Return to the applicant

The applicant will be advised to shift the application path way or provide additional documents if the application is found ineligible for this approval pathway. However, submitting fabricated data will end up in rejecting the application or all applications from the same manufacturer based on the severity of consequences of the fabricated data.

c) Review of documents

Completeness and validity of all submitted documents and selected technical sections of the documents should be evaluated by taking product-specific characteristics in to considerations. These includes specifications, analytical methods, manufacturing process and process controls, stability studies, and certificate of analysis.

7 Post approval Changes and Re-registration applications

7.1 Variation

For post approval variations, the applicants are advised to submit compulsory sections of the documents in line with the requirements of **the guideline for submission of post approval variation application**. Whenever a product has been withdrawn from the market and/or its marketing authorization has been rejected, deferred, or withdrawn from market for any reason (such as deficiencies in GMP, product quality defect or ADE reports) in other countries, the local agent or the manufacturer should notify EFDA as per the article 67(17) of proclamation No 1112/2019.

7.2 Re- Registration

Applications for re-registration of products with therapeutic claim shall follow requirements specified in Appendix 4 (Requirements for Re-registration) of the Authority`s guideline for registration of medicines, 4th Edition, 2020**.**

Annex I: List of oral care and skin care products with therapeutic claim

1. Skin care products
   - Anti-acne
     - Benzoyl peroxide in concentrations of 2.5 to 10.0%
     - Salicylic acid in concentrations of 0.5 to 2.0%
     - Sulfur in concentrations of 3.0 to 10.0 %
     - Resorcinol in 2.0 % concentration in combination with sulfur in concentrations of 3.0 to 8.0%.
     - Resorcinol monoacetate in 3.0 % concentration in combination with sulfur in concentrations of 3.0% to 8.0 %.
   - anti-nappy rash treatments
   - Emollient/ demulcent with therapeutic claims (eg. To relief itching)
   - medicated soaps
   - skin protectants with therapeutic claim
   - sunscreens Sunscreen ingredients eligible for regulation by this guideline.
     - Aminobenzoic acid (PABA) up to 15%
     - Avobenzone up to 3%
     - Cinoxate up to 3%
     - Dioxybenzone up to 3%
     - Homosalate up to 15%
     - Menthyl anthranilate up to 5%
     - Octocrylene up to 10%
     - Octyl methoxycinnamate up to 7.5%
     - Octyl salicylate up to 5%
     - Oxybenzone up to 6%
     - Padimate O up to 8%
     - Phenylbenzimidazole sulfonic acid up to 4%

- Sulisobenzone up to 10%
- Titanium dioxide up to 25%
- Trolamine salicylate up to 12%
- Zinc oxide up to 25%
- Ensulizole up to 4%
- Homosalate up to 15%
- Meradimate up to 5%
- Octinoxate up to 7.5%
- Octisalate up to 5%
- Octocrylene up to 10%
- Oxybenzone up to 6%
- Padimate O up to 8%

2. Oral care products includes

   – Anesthetic, astringent, antimicrobial, debriding, demulcent, expectorant, decongestant desensitizing toothpastes and gels with fluoride content >1500ppm

   – Antigingivitis/Antiplaque

   – lozenges for soothing dry throat

   – oral mucosal analgesics

   – oral mucosal protectant

   – Therapeutic mouth rinses

   – Tooth ache relief

   – Tooth desensitizer

Annex II: Application form for registration of oral care and skin care product

Food and Drug Authority of Ethiopia

P.O. Box 5681, Addis Ababa, Ethiopia

1. Name of the finished product:_____
2. Dosage form: _____
3. Description of the product:_____
4. Presentation (pack size, content):_____
5. Shel life (months): _____
6. Composition of the product

Composition of the finished product per ___			
S.No	Name of ingredient	Strength (mg, %)	Function
1			
2			
3			
4			

7. Main indication:_____

   _____

   _____

8. Manufacturer

   Name of the manufacturer:_____

   Street Address:_____

   Plant address: _____

   Postal Address: _____

   Tel. number: _____

   Fax number:_____

Email: _____

9. Local agent (representative) in Ethiopia

   Name: _____

   Street Address: _____

   Postal address:_____

   Tel. number: _____

   Fax number: _____

   E-mail: _____

10. Supporting Documents or materials attached (List them and annotate)

_____

_____

_____

_____

_____

Name of contact person in the manufacturer: _____

Official designation:_____

Professional status (position held): _____

Signature: _____