Maldives Food and Drug Authority

Ministry of Health

Male', Maldives

Guideline for Pre-Authorization Approval of Medicines

Guideline for Pre-authorization Approval of Medicines is released under the authority of

Ms. Thooma Adam
Health Laboratory Specialist (Acting Head, MFDA)
Maldives Food and Drug Authority

It is the property of:
Maldives Food and Drug Authority
Male'
Republic of Maldives

Document Approved by:
Aishath Mohamed
Pharmaceutical Specialist

Document Verified by Technical Committee, Medicine and Therapeutic Goods Division.

Document Prepared By:

Fathimath Azla
Pharmaceutical Officer

Contents

ABBREVIATIONS

GMP	Good Manufacturing Practices
CoPP	Ceritificate of Pharmaceutical Product
COA	Certificate of Analysis
MFDA	Maldives Food and Drug Authority
MTG	Medicine and Therapeutics Goods Division
PA	Pre-Authorization
ADL	Approved Drugs List
HPA	Health Protection Agency
WHO	World Health Organization

Definitions

Applicant	The person or Company who submits an application of a product to the Authority and is responsible for the product information, recall etc., availability.
Importer	Company/sole proprietorship/partnerships registered as an importer in MFDA with a valid Importers Permit. Preauthorisation approval can be only requested by a registered importer.
Manufacturer of the Product	A company that carries out all the operations of production, packaging, labeling and quality assurance of the products.
Product Label	Includes all the written, printed or graphic material of the primary and secondary packaging of the product, excluding any outer shipping container.
Evaluation	Refers to a comprehensive safety, efficacy and quality analysis of the submitted product for registration.
Good Manufacturing Practices (GMP)	Refers to a system which ensures that products are consistently produced and controlled according to quality standards (WHO).
Approved Drug List (ADL)	A list of all medicinal products approved for import and use in Maldives.
Batch	A defined quantity of product processed in a single process or series of processes and therefore expected to be homogeneous. In continuous manufacture, the batch must correspond to a defined fraction of production, characterized by its intended homogeneity. Source: World Health Organization WHO Technical Report Series, No. 863, 1996
Post market surveillance	Post market surveillance, is the practice of monitoring the safety of a medicine after it has been released on the market and is an important part of the science of pharmacovigilance. Since these medicines are approved on the basis of registration, post-market surveillance can further evaluate the safety of a medicine after it is used in the general population by large numbers of people who have a wide variety of medical conditions.

1 INTRODUCTION

Maldives is a 100% importing country for medicines. Due to the small market and due to low volume of critically required medicines, importers are unable to get the required documentation from manufacturers for registration of these products.

However, as these medicines are required for the health care system, MFDA has established preauthorization approvals as an exemption approval after evaluating the minimum safety requirements of the product.

This approval is only given for essential medicines and the main purpose of this approval is to ensure availability and accessibility of these essential medicines including critical and emergency medicines antidotes. For this approval a full dossier of the product is not required.

In the Approved Drug List, products eligible for this approval is categorized as “Pre-Authorization required before import” (highlighted in green).

As this is a Pre-Authorization, (Not a Post Authorization), the products which are already imported will not be included for this approval.

2 Purpose

This guideline has been developed as a guidance for all medicines importers on preauthorization application and approval process.

3 Stakeholders

Medicine importers responsible for taking PA before import	Only registered medicine importer can apply for a PA
Health Protection Agency (HPA)	An approval is given for National immunization program conducted by HPA
World Health Organization (WHO)	An approval is given for Donation medicines
Pharmacists/Pharmacy owners	Inform any product safety issues and corporate any recall issues.
Consumers	Main users of medicine

4 Requirements for Applications

4.1.1 The applicant shall be registered as an authorized medicine importer under the authority as per the criteria of medicine regulation R-46/2014 & R-49/2016 with valid importers permit from MTG/MFDA.

4.1.2 The importer shall have an established system for reporting and handling adverse drug reaction (ADR). Evidence of this shall be submitted when registering as an authorized medicine importer.

All electronic documents submitted shall be signed and endorsed by the concerned regulatory authorities. If the submitted documents are not signed and endorsed it can be accepted only if it can be verified from the relevant regulatory authorities.

4.1.3 All documents submitted shall be in English language.

4.1.4 MTG/MFDA will reject the applications which does not fulfill the required criteria as mentioned above.

4.1.5 For all the pediatric oral formulations including cough, cold and paracetamol formulations, the certificate of analysis (COA) shall be submitted for all the excipients used, specifically if glycerin or glycerol or propylene glycol (sorbitol) is used, verifying that it does not contain the impurities diethylene glycol (DEG) and ethylene glycol (EG).

4.1.6 Manufacture validation protocols of the excipients shall be submitted specifically those that are at a risk for diethylene glycol (DEG) and ethylene glycol (EG) contamination. For such excipients each container of the excipients shall be tested for purity and validity and evidence documents shall be submitted.

4.1.7 Nitrosamine impurities are compounds containing a nitroso group at the dialkyl-substituted amine group. In RANITIDINE, Valsartan, Losartan, and Irbesartan substances, these impurities result from the reaction of solvent impurities (used for synthesis) and nitrite ions in the acidic environment. NDMA contamination poses a potential carcinogenic risk. The product shall be tested for purity and validity and evidence documents shall be submitted during import for the specific batch imported at that time.

5 How to Apply

5.1.1 Application shall be submitted online via MFDA's Dhirithi portal (https://dhirithi.egov.mv).

5.1.2 In order to do so, the importer shall first register as a user in Dhirithi portal using the form available on the MOH website and in Dhrithi portal under "Publications".

5.1.3 The product applied for must be a product that has been previously not approved for PA and categorized as a PA required product in the most recent version of ADL.

5.1.4 Control medicines and hospital use products can only be requested by MTG/MFDA designated importers.

5.1.5 For this approval minimum documents are required to ensure the quality safety, efficacy of the product.

5.1.6 If all requirements are met PA is issued for a duration of 3 years.

6 Documents and Acceptance Criteria of the documents

6.1 Pharmaceutical Information Sheet

6.1.1 Brand name, Trade name or Product name shall tally with COPP submitted.

6.1.2 If more than one active ingredient is present in the preparation, it shall be separated by a + between each active ingredients (eg: *Calcium carbonate + Docosahexaenoic Acid + vitamin) Strength: 500mg + 150mg + D3 200IU)*

6.1.3 The intended use or the indication of the product shall be clearly specified. *Example: Used for upper respiratory infections*

6.1.4 All routes of administration proposed for the product shall be included and specified accordingly.

6.1.5 Therapeutic Class according to WHO ATC Index shall be indicated with:

1) The WHO ATC code
2) WHO ATC classification
3) Shall be provided for each therapeutic indication proposed for a product.

6.1.6 Full address of the manufacturer shall be provided with site and country of origin.

6.1.7 Storage conditions of the product shall be provided:

a) The condition in which product shall be stored and kept shall be clearly specified. *Example temperature, humidity etc. of the product storage shall be specific.*

6.2 Valid GMP certificate

6.2.1 Proof of GMP compliance (valid GMP certificate) shall be submitted for all the sites relevant to the product.

6.2.2 A color scanned copy of the original or certified true copy of GMP certification document issued by the relevant drug regulatory agency shall be submitted, certifying that the manufacturer concerned complies with current applicable GMP standard.

6.2.3 GMP Certificate shall have the following information; date of issue, identity of issuing authority or agency approving GMP certificate, validity of the GMP, manufacturing site address and dosage forms of productions.

6.2.4 GMP Certificate shall have the validity of 6 months at the time of submission.

6.2.5 If the GMP does not have the 6-month validity, the client shall submit proof document requesting to renew the GMP from the country of origin and hence these applications shall be put on hold till the new GMP is submitted. Once the new GMP certificate is submitted, approval of the product will be processed.

6.2.6 If the validity period or expiry date is not stated on the GMP Certificate, the applicant shall supply supporting documents to confirm the validity period of the GMP certificate.

6.2.7 The specific dosage form applied for PA approval shall be mentioned in the GMP.

6.3 Certificate of a Pharmaceutical Product (CoPP)

6.3.1 CoPP shall be in the format of the WHO Certification Scheme on the Quality of Pharmaceutical Products.

6.3.2 A color scanned copy of the original or certified true copy of CoPP certification document issued by the relevant drug regulatory authority of the country of origin shall be submitted which necessarily does not require to be country specific.

6.3.3 CoPP Certificate shall have validity of 6 months from the time of submission of the application.

6.3.4 If the certificate is nearing its expiry, evidence of application or under process letter for renewal issued by the same licensing authority shall be submitted along with the current CoPP.

a) If the expiry of the CoPP is not mentioned in the certificate, evidence document shall be submitted for assurance of the validity.

6.4 Certificate of Analysis for batch release/Certificate of Analysis of Finished Product (CoA)

6.4.1 This certificate Shall be a notarized true copy.

6.4.2 This certificate Shall contain the following information:

a) Name and address of the certifying/notarizing authority

b) Batch details

6.4.3 Batch analyses data from a minimum of 2 batches shall be submitted for the product submitted for PA approval.

6.4.4 Shall include a conclusion specifying that the product is in compliance.

6.5 Product Label

6.5.1 Product label shall contain the following information;

a. Brand name, Generic name, strength and dosage form.

b. Full manufacturing site address of the product.

c. Exemptions: In case if the manufacturer is not defined in the label for category1 manufactured product, a specific code shall be in the label to trace the manufacture name and address and this shall tally with the submitted document.

d. Special precaution if applicable

e. Shelf life

f. Storage condition

g. Shall be submitted in English

h. Picture of the product covering all the sides.

i. The draft artwork of the outer carton labels shall be in the actual format, design and colour that are to be printed.

6.6 Company profile

6.6.1 The product must be manufactured by a manufacturer already registered in the ADL, or the product shall be from category 1. If not, the application will be rejected. The following documents shall be submitted if the product is from the category 1:

a. A brief description of the manufacturer, when it was established and the products manufactured shall be submitted.

b. Shall Provide a short description of accreditations, achievements and standards practiced of the manufacturer

c. Shall Provide list of products manufactured and specify those currently marketed in the country of origin.

d. Shall provide a list of products manufactured and exported to other countries, specifying which products are exported to which country.

7 Application Processing

7.1.1 Once the applicant requests, it will be checked for document completion and legibility. If all the requirements as per the acceptance criteria is fulfilled, then only the request will be accepted within 10 working days.

7.1.2 MFDA shall have the right to reject incomplete applications and hence it's the applicant's responsibility to ensure that all are in accordance with the requirements.

7.1.3 If all the requirements are complete, the request will be accepted and requests that require further clarification will be put to "Need clarification" status on Dhirithi portal. The clarification requested by the authority shall be resolved within 10 working days by the applicant, otherwise the request will be rejected.

7.1.4 In the case of a rejection, the reason for the rejection will be specified.

7.1.5 An Invoice will be generated with a fee of 7710/- MVR (Seven Thousand Seven Hundred and Ten Maldivian Rufiyaa) which shall be paid via Bandeyri Pay within 5 working days from the time of status change to "verified" in Dhirithi portal. If the payment is not made within the given 5 days, the request will be rejected. This fee is non-refundable.

7.1.6 All financial transactions will be processed through Bandeyri Pay and MTG/MFDA will not request for or accept any other methods of payment.

7.1.7 The PA approval process may be prolonged due to the time taken by the applicant to respond to the authority's request to provide additional information or further clarification.

8 Issuing the PA permit

8.1.1 Once the payment is made the request will be approved and status will be updated from Dhirithi portal as "Approved".

8.1.2 Once the request is approved, a signed copy of the PA permit will be uploaded to Dhirithi portal within 2 working days from the date of Approval.

8.1.3 The product can only be imported, distributed and sold in the country once the pre-authorization approval has been issued and permit has been uploaded to Dhirithi portal.

8.1.4 A format of the permit is in the Annex 1.

9 Authorizations for National Programs, and Donations.

9.1.1 Health Protection Agency (HPA) is the responsible body for ensuring the availability of National program Medicines for the Maldives.

9.1.2 The product shall be a WHO pre-qualified product and shall apply with a proof the product is WHO pre-qualified.

9.1.3 If 9.1.2 is unavailable, a copy of GMP certification document and a copy of CoPP document issued by the relevant drug regulatory agency shall be submitted.

9.1.4 Product label shall contain the following information;

- Brand name, Generic name, strength and dosage form
- Full manufacturing site address of the product.
- Shall be in English language.

9.1.5 This approval is issued for 1 year if all the requirements are fulfilled.

9.1.6 A permit is not required for the products already mentioned in the Approved Drug List

9.1.7 If the brand name, strength, dosage form or the manufacturer is different than section 9.1.6, a permit is required as of section 9.1.2.

9.1.8 A format of the permit is in the Annex 1.

10 Responsibilities of Importers with PA Approvals

10.1.1 The importer shall take full responsibility of the medicine that is going to be in the market, which includes, informing the authority of any variations in the product after issuance of PA, recalling the medicine (PA taken and imported) if required.

10.1.2 If any quality issue of the product imported is identified, MTG/MFDA has the right to revoke the permit at any time. In addition, the product and the manufacturer will be on hold for further imports until the investigation is completed.

10.1.3 If there is any recall notification from MTG/MFDA, the importer shall take the responsibility to recall the product from the market and proceed with disposal as per the instruction of the MFDA.

11 Re-registration process of a pharmaceutical product

11.1.1 Once the 3-year duration of PA permit is complete, the same product cannot be given PA approval for a second time. The product has to be registered as per the re-registration criteria as mentioned in section 11.1.4.

11.1.2 Within 3 years period, at least TWO batches which they have imported shall be tested from a WHO prequalified laboratory or from an accredited laboratory of a category 1 country and this test report shall be submitted.

11.1.3 Any details of the product shall not differ from the initial documents at time of submission.

11.1.4 Product registration process will be conducted according to Guideline on Product Registration and Approval of Medicines (MTG/RE-RP/GLN-TE 001), section 16.2.1

Code	Document to be submitted
B	Pharmaceutical Information Sheet
C61	Valid GMP certificate
D3	Valid Certificate of a Pharmaceutical Product (CoPP)
E2	Copy of the Finished Product specification
F12 (2.1)	Accelerated Stability Data
F12 (2.2)	Real-Time/Long-term Stability Data
H5	Product Label/Packing insert
I1	Cost and Retail price
12	Submitting Periodic safety update reports (PSURs) for the PA period (3 years)

Note: Prior to the effective date of this guideline, PA approvals were issued for a duration of one year and renewed for additional 2 years. The process required for these approvals is detailed in the Annex 2 of this guideline.

12 Rejection, Cancellation or Suspension of PA approval

12.1.1 The Maldives Food and Drug Authority reserves the right to reject, cancel or suspend the approval of any product if:

a. There are deficiencies in safety, quality, or efficacy of the product

b. Failure to comply with conditions of Approval.

c. Any report on adverse drug reactions of serious nature has been received from national or international sources.

d. Failure to submit the mandatory documents.

13 Pre market and Post Market Testing

13.1.1 Once the product is PA approved, imported and introduced to the market, the product shall be on surveillance as to ensure that the same product PA taken is in the market.

13.1.2 National Health Laboratory (NHL) is the designated national laboratory for testing pharmaceuticals.

13.1.3 Once a PA product is imported and introduced to the market, as part of the post market surveillance, samples will be collected from the market and tested from NHL as well as the designated laboratory from abroad and these results will be published.

13.1.4 MFDA will put the company on surveillance for any recalls or alerts of any products manufactured by that company.

14 Legal basis

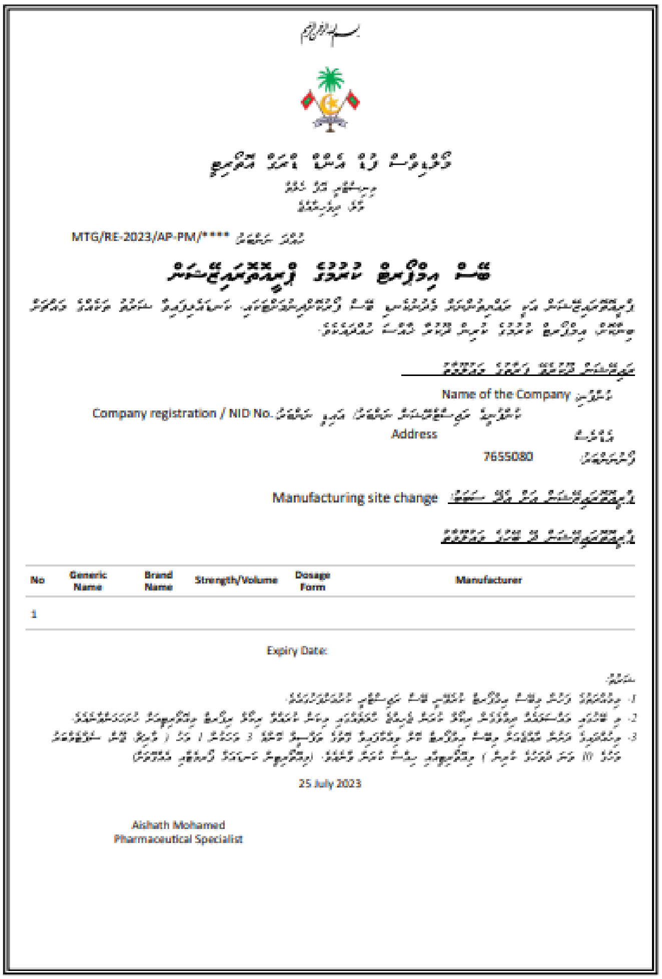
1. Medicine Regulation R-46 (2014)
2. Medicine Regulation Amendment R-49 (2016)
3. Health Service Act (29/2015)

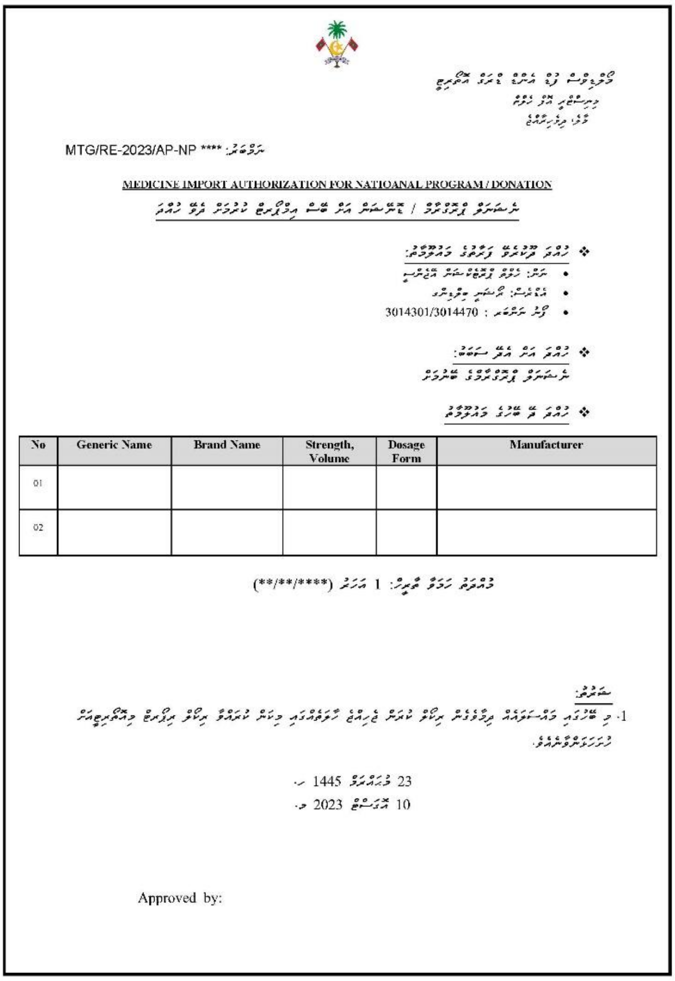
15 Annex

Annex 1: Pre-authorization Approval

Annex 2: Note for existing pre-authorization permits (prior to effective date of this guideline)

Annex-1


MTG/RE-2023/AP-PM/****
Name of the Company
Company registration / NID No.
Address
7655080
Manufacturing site change
No
Generic Name
Brand Name
Strength/Volume
Dosage Form
Manufacturer
1
Expiry Date:
25 July 2023
Aishath Mohamed
Pharmaceutical Specialist


MTG/RE-2023/AP-NP ****
MEDICINE IMPORT AUTHORIZATION FOR NATIOANAL PROGRAM / DONATION
3014301/3014470
No
Generic Name
Brand Name
Strength, Volume
Dosage Form
Manufacturer
01
02
(**/**/****)
23 1445
10 2023
Approved by:

Annex: 2

Existing Pre-Authorizations

Prior to the effective date of this guideline, preauthorization approvals were given for one year for new PA applications. For these permits the process will be as follows:

- Prior to the completion of the one-year period the importer shall submit a request for renewing the PA Approval, which should be in the Approved Drug List as PA required.
- If the renewal is requested within the one year, and is in ADL as Pre-authorization required product, the approval is renewed for further two years period without any payment requirements.
- After these two years are completed the process for re-registration has to be followed as stated in point 11 of this guideline.