Zambia Medicines Regulatory Authority

APPLICATION FOR MARKETING AUTHORISATION OF A MEDICINE FOR HUMAN USE

COMMON TECHNICAL DOCUMENT FORMAT

- **ZAMBIA Module 1**
- **CTD-Modules 2 - 5**

Version 03, April 2015

ZAMBIA Common Technical Document

Modular format of applications for registration in CTD format

ZAMBIA Module 1 — Administrative information and prescribing information

1.0 Cover Letter

1.1 Comprehensive table of contents

1.2 Application Information

1.2.1 Application form

1.2.2 Letter of authorisation for communication on behalf of the applicant

1.2.3 Electronic copy declaration

1.2.4 Copy of certificate for a Vaccine Antigen Master File (VAMF)

1.2.5 Copy of certificate for a Plasma Master File (PMF)

1.2.6 Copy of certificate(s) of suitability of the European Pharmacopoeia (CEP)

1.2.7 Copy of confirmation of API prequalification document (CPQ)

1.2.8 Letter of access from APIMF, CEP or CPQ holder

1.3 Labelling and packaging

1.3.1 Package Insert

1.3.2 Summary of Product Characteristics (SmPC)

1.3.3 Patient Information Leaflet (PIL)

1.3.4 Labels (outer and inner labels)

1.3.5 Braille

1.4 Information about the experts

1.4.1 Quality

1.4.2 Non-clinical

1.4.3 Clinical

1.5 Specific requirements for different types of applications

1.5.1 Studies and data for generic products

1.6 Environmental risk assessment

1.7 Good manufacturing practice

1.7.1 Date of last inspection of each site

1.7.2 Inspection reports or equivalent document

1.7.3 Latest GMP certificate (not older than 3 years) for API and FPP manufacturer/s and packer/s or a copy of the appropriate manufacturing licence

1.7.4 Registration of Responsible Pharmacist or Suitably Qualified Person for local manufacturers

1.7.5 Certified copy of a permit to manufacture specified controlled substances

1.8 Details of Screening

1.9 Individual patient data - statement of availability, if applicable

1.10 Foreign regulatory status

1.10.1 List of SADC or other countries in which an application for the same product as being applied for has been submitted, registered, rejected or withdrawn.

1.10.2 WHO type Certificate of Pharmaceutical Product (COPP)

1.10.3 Registration certificate or marketing authorisation

1.10.4 Foreign prescribing and patient information

1.10.5 Data set similarities

1.11 Regional Summaries

1.11.1 Summary of the Bioequivalence Studies

1.11.1.1 Study Title(s) (or brief description giving design, duration, dose and subject population of each study)

1.11.1.2 Protocol and study numbers

1.11.1.3 Investigational products (test and reference) details

1.11.1.4 Confirmation that the test product formulation and manufacturing process is that being applied for

1.11.1.5 Name and address of the Research Organisation(s) / Contract Research Organisation(s) where the bioequivalence studies were conducted

1.11.1.6 Sponsor and responsible sponsor representative: name and address, contact details

1.11.1.7 Duration of Clinical phase: dates of dosing and last clinical procedure

1.11.1.9 Date of final report

1.11.2 Biostudy reference product confirmation

1.11.3 Certificates of analysis of the test and reference products

1.11.4 Bioequivalence trial information form (or BTIF)

1.11.5 Biowaiver requests in relation to conducting comparative bioavailability study

1.11.6 Quality Information Summary (QIS)

1.12 Paediatric development programme

1.13 Information relating to Pharmacovigilance

1.13.1 Pharmacovigilance system

1.13.2 Risk management system

1.14 Electronic review documents (e.g. product information, BTIF, QOS)

1.15 Sample and Documents (e.g. FPP, device(s), certificates of analysis)

1.15.1 Confirmation of submission of sample

1.15.2 Certificate of analysis of the sample

Module 2 - CTD Summaries

2.1 CTD Table of Contents (modules 2 to 5)

2.2 Introduction

2.3 Quality Overall Summary - Introduction

2.3.S Quality Overall Summary – Drug Substance / Active Pharmaceutical Ingredient *(name, manufacturer)*

2.3.S.1 General Information *(name, manufacturer)*

2.3.S.2 Manufacture *(name, manufacturer)*

2.3.S.3 Characterisation *(name, manufacturer)*

2.3.S.4 Control of Drug Substance /Active Pharmaceutical Ingredient *(name, manufacturer)*

2.3.S.5 Reference Standards or Materials *(name, manufacturer)*

2.3.S.6 Container Closure System *(name, manufacturer)*

2.3.S.7 Stability *(name, manufacturer)*

2.3.P Quality Overall Summary – Drug Product / Finished Pharmaceutical Product *(name, dosage form)*

2.3.P.1 Description and Composition of the Drug Product / Pharmaceutical Product *(name, dosage form)*

2.3.P.2 Pharmaceutical Development *(name, dosage form)*

2.3.P.3 Manufacture *(name, dosage form)*

2.3.P.4 Control of Excipients *(name, dosage form)*

2.3.P.5 Control of Drug Product / Pharmaceutical Product *(name, dosage form)*

2.3.P.6 Reference Standards or Materials *(name, dosage form)*

2.3.P.7 Container Closure System *(name, dosage form)*

2.3.P.8 Stability *(name, dosage form)*

2.3.A Quality Overall Summary - Appendices

2.3.A.1 Facilities and equipment *(name, manufacturer)*

2.3.A.2 Adventitious agents safety evaluation *(name, dosage form, manufacturer)*

2.3.A.3 Excipients

2.4 Non-clinical Overview

2.5 Clinical Overview

2.5.1 Product Development Rationale

2.5.2 Overview of Bio pharmaceutics

2.5.3 Overview of Clinical Pharmacology

2.5.4 Overview of Efficacy

2.5.5 Overview of Safety

2.5.6 Benefits and Risks Conclusions

2.5.7 Literature References

2.6 Non-clinical Written and Tabulated Summaries

2.6.1 Introduction

2.6.2 Pharmacology Written Summary [1]

2.6.2.1 Brief Summary

2.6.2.2 Primary Pharmacodynamics

2.6.2.3 Secondary Pharmacodynamics

2.6.2.4 Safety Pharmacology

2.6.2.5 Pharmacodynamic Medicine Interactions

2.6.2.6 Discussion and Conclusions

2.6.2.7 Tables and Figures (See Appendix A)

2.6.3 Pharmacology Tabulated Summary (See Appendix B)

2.6.4 Pharmacokinetics Written Summary [2]

[1] *The CTD defines these further heading levels and navigation should be provided within the document to these subheadings.*

2.6.4.1 Brief Summary

2.6.4.2 Methods of Analysis

2.6.4.3 Absorption

2.6.4.4 Distribution

2.6.4.5 Metabolism (interspecies comparison)

2.6.4.6 Excretion

2.6.4.7 Pharmacokinetic Medicine Interactions

2.6.4.8 Other Pharmacokinetic Studies

2.6.4.9 Discussion and Conclusions

2.6.4.10 Tables and Figures (See Appendix A)

2.6.5 Pharmacokinetics Tabulated Summary (See Appendix B)

2.6.6 Toxicology Written Summary [2]

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2.6.6.2 Single-Dose Toxicity

2.6.6.3 Repeat-Dose Toxicity (including supportive toxicokinetics evaluations)

2.6.6.4 Genotoxicity

2.6.6.5 Carcinogenicity (including supportive toxicokinetics evaluations)

2.6.6.6 Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations)

2.6.6.7 Local Tolerance

2.6.6.8 Other Toxicity Studies (if available)

2.6.6.9 Discussion and Conclusions

2.6.6.10 Tables and Figures (See Appendix A)

2.6.7 Toxicology Tabulated Summary (See Appendix B)

2.7 Clinical Summary

2.7.1 Summary of Biopharmaceutical Studies and Associated Analytical Methods [2]

2.7.1.1 Background and Overview

2.7.1.2 Summary of Results of Individual Studies

2.7.1.3 Comparison and Analyses of Results Across Studies

2.7.1.4 Appendix

2.7.2 Summary of Clinical Pharmacology Studies [3]

2.7.2.1 Background and Overview

2.7.2.2 Summary of Results of Individual Studies

[2] *The CTD defines these further heading levels and navigation should be provided within the document to these subheadings.*

2.7.2.3 Comparison and Analyses of Results Across Studies

2.7.2.4 Special Studies

2.7.2.5 Appendix

2.7.3 Summary of Clinical Efficacy – *Indication* [3]

2.7.3.1 Background and Overview of Clinical Efficacy

2.7.3.2 Summary of Results of Individual Studies

2.7.3.3 Comparison and Analyses of Results Across Studies

2.7.3.3.1 Study Populations

2.7.3.3.2 Comparison of Efficacy Results of All Studies

2.7.3.3.3 Comparison of Results in Sub-populations

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2.7.3.6 Appendix

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2 7.4.1.1 Overall Safety Evaluation Plan and Narratives of Safety Studies

2 7.4.1.2 Overall Extent of Exposure

2 7.4.1.3 Demographic and Other Characteristics of Study Population

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2.7.4.2.1.1 Common Adverse Events

2.7.4.2.1.2 Deaths

2.7.4.2.1.3 Other Serious Adverse Events

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2.7.4.2.1.5 Analysis of Adverse Events by Organ System or Syndrome

2.7.4.2.2 Narratives

2.7.4.3 Clinical Laboratory Evaluations

2.7.4.4 Vital Signs, Physical Findings and Other Observations related to Safety

2.7.4.5 Safety in Special Groups and Situations

2.7.4.5.1 Intrinsic Factors

2.7.4.5.2 Extrinsic Factors

2.7.4.5.3 Medicine Interactions

2.7.4.5.4 Use in Pregnancy and Lactation

2.7.4.5.5 Overdose

2.7.4.5.6 Medicine Abuse

2.7.4.5.7 Withdrawal and Rebound

2.7.4.5.8 Effects on Ability to Drive of Operate Machinery or Impairment of Mental Ability

2.7.4.6 Post-marketing Data

2.7.4.7 Appendix

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2.7.6 Synopses of Individual Studies

Module 3 - Quality

3.1 Table of contents of module 3

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3.2.S Drug Substance / Active Pharmaceutical Ingredient *(name, manufacturer)*

3.2.S.1 General information (name, manufacturer)

3.2.S.1.1 Nomenclature *(name, manufacturer)*

3.2.S.1.2 Structure *(name, manufacturer)*

3.2.S.1.3 General Properties *(name, manufacturer)*

3.2.S.2 Manufacture (name, manufacturer)

3.2.S.2.1 Manufacturer(s) *(name, manufacturer)*

3.2.S.2.2 Description of Manufacturing Process and Process Controls *(name, manufacturer)*

3.2.S.2.3 Control of Materials (name, manufacturer)

3.2.S.2.4 Controls of Critical Steps and Intermediates (name, manufacturer)

3.2.S.2.5 Process Validation and/or Evaluation (name, manufacturer)

3.2.S.2.6 Manufacturing Process Development *(name, manufacturer*)

3.2.S.3 Characterisation *(name, manufacturer)*

3.2.S.3.1 Elucidation of Structure and other Characteristics *(name, manufacturer)*

3.2.S.3.2 Impurities *(name, manufacturer)*

3.2.S.4 Control of active pharmaceutical ingredient *(name, manufacturer)*

3.2.S.4.1 Specifications *(name, manufacturer)*

3.2.S.4.2 Analytical Procedures *(name, manufacturer)*

3.2.S.4.3 Validation of Analytical Procedures *(name, manufacturer)*

3.2.S.4.4 Batch Analyses *(name, manufacturer)*

3.2.S.4.5 Justification of Specification *(name, manufacturer)*

3.2.S.5 Reference Standards or Materials *(name, manufacturer)*

3.2.S.6 Container Closure System *(name, manufacturer)*

3.2.S.7 Stability (name, manufacturer)

3.2.S.7.1 Stability summary and conclusions *(name, manufacturer)*

3.2.S.7.2 Post approval stability protocol and stability commitment *(name, manufacturer)*

3.2.S.7.3 Stability Data *(name, manufacturer)*

3.2.P Drug Product / Pharmaceutical Product *(name, dosage form)*

3.2.P.1 Description and Composition of the Drug Product / pharmaceutical product *(name, dosage form)*

3.2.P.2 Pharmaceutical Development *(name, dosage form)*

3.2.P.2.1 Components of the Drug Product / Pharmaceutical Product *(name, dosage form)*

3.2.P.2.1.1 Drug Substance / Active Pharmaceutical Ingredient(s) *(name, dosage form)*

3.2.P.2.1.2 Excipients *(name, dosage form)*

3.2.P.2.2 Final Drug Product / pharmaceutical product *(name, dosage form)*

3.2.P.2.2.1 Formulation development *(name, dosage form)*

3.2.P.2.2.2 Overages *(name, dosage form)*

3.2.P.2.2.3 Physicochemical and biological properties *(name, dosage form)*

3.2.P.2.3 Manufacturing process development *(name, dosage form)*

3.2.P.2.4 Container closure system *(name, dosage form)*

3.2.P.2.5 Microbiological attributes *(name, dosage form)*

3.2.P.2.6 Compatibility *(name, dosage form)*

3.2.P.3 Manufacture *(name, dosage form)*

3.2.P.3.1 Manufacturer(s) *(name, dosage form)*

3.2.P.3.2 Batch formula *(name, dosage form)*

3.2.P.3.3 Description of manufacturing process and process controls *(name, dosage form)*

3.2.P.3.4 Controls of critical steps and intermediates *(name, dosage form)*

3.2.P.3.5 Process validation and/or evaluation *(name, dosage form)*

3.2.P.4 Control of Inactive Pharmaceutical Ingredients *(name, dosage form)*

3.2.P.4.1 Specifications *(name, dosage form)*

3.2.P.4.2 Analytical procedures *(name, dosage form)*

3.2.P.4.3 Validation of analytical procedures *(name, dosage form)*

3.2.P.4.4 Justification of specifications *(name, dosage form)*

3.2.P.4.5 Excipients of human or animal origin *(name, dosage form)*

3.2.P.4.6 Novel excipients *(name, dosage form)*

3.2.P.5 Control of Drug Product / pharmaceutical product *(name, dosage form)*

3.2.P.5.1 Specification(s) *(name, dosage form)*

3.2.P.5.2 Analytical procedures *(name, dosage form)*

3.2.P.5.3 Validation of analytical procedures *(name, dosage form)*

3.2.P.5.4 Batch analyses *(name, dosage form)*

3.2.P.5.5 Characterisation of impurities *(name, dosage form)*

3.2.P.5.6 Justification of specifications *(name, dosage form)*

3.2.P.6 Reference standards or materials *(name, dosage form)*

3.2.P.7 Container closure system *(name, dosage form)*

3.2.P.8 Stability (name, dosage form)

3.2.P.8.1 Stability summary and conclusion *(name, dosage form)*

3.2.P.8.2 Post-approval stability protocol and stability commitment *(name, dosage form)*

3.2.P.8.3 Stability data *(name, dosage form)*

3.2.A Appendices

3.2.A.1 Facilities and equipment *(name, manufacturer)*

3.2.A.2 Adventitious agents safety evaluation *(name, dosage form, manufacturer)*

3.2.A.3 Excipients

3.2.R Regional Information

3.2.R.1 Production documentation

3.2.R.1.1 Executed production documents

3.2.R.1.2 Master production documents

3.2.R.2 Analytical procedures and validation information

3.3 Literature references

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4.2 Study reports

4.2.1 Pharmacology

4.2.1.1 Primary pharmacodynamics

4.2.1.2 Secondary pharmacodynamics

4.2.1.3 Safety pharmacology

4.2.1.4 Pharmacodynamic medicine interactions

4.2.2 Pharmacokinetics

4.2.2.1 Analytical methods and validation reports

4.2.2.2 Absorption

4.2.2.3 Distribution

4.2.2.4 Metabolism

4.2.2.5 Excretion

4.2.2.6 Pharmacokinetic medicine interactions (non clinical)

4.2.2.7 Other pharmacokinetic studies

4.2.3 Toxicology

4.2.3.1 Single-dose toxicity (in order by species, by route)

4.2.3.2 Repeat dose toxicity (in order by species, by route, by duration; including supportive toxicokinetics evaluations)

4.2.3.3 Genotoxicity

4.2.3.3.1 *In vitro*

4.2.3.3.2 *In vivo (*including supportive toxicokinetics evaluations)

4.2.3.4 Carcinogenicity (including supportive toxicokinetics evaluations)

4.2.3.4.1 Long-term studies (in order by species, including range-finding studies that cannot be appropriately included under repeat-dose toxicity or pharmacokinetics)

4.2.3.4.2 Short or medium term studies (including range finding studies that cannot be appropriately included under repeat-dose)

4.2.3.4.3 Other studies

4.2.3.5 Reproductive and developmental toxicity (including range-finding studies and supportive toxicokinetics evaluations) (If modified study designs are used, the following subheadings should be modified accordingly)

4.2.3.5.1 Fertility and early embryonic development

4.2.3.5.2 Embryo-foetal development

4.2.3.5.3 Prenatal and postnatal development, including maternal function

4.2.3.5.4 Studies in which the offspring (juvenile animals) are dosed and/or further evaluated

4.2.3.6 Local tolerance

4.2.3.7 Other toxicity studies (if available)

4.2.3.7.1 Antigenicity

4.2.3.7.2 Immunotoxicity

4.2.3.7.3 Mechanistic studies (if not included elsewhere)

4.2.3.7.4 Dependence

4.2.3.7.5 Metabolites

4.2.3.7.6 Impurities

4.2.3.7.7 Other

4.3 Literature references

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5.1 Table of contents of Module 5

5.2 Tabular listing of all clinical studies

5.3 Clinical study reports

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5.3.1.2 Comparative BA and Bioequivalence (BE) Study Reports

5.3.1.3 *In vitro-in vivo* correlation study reports

5.3.1.4 Reports of bioanalytical and analytical methods for human studies

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5.3.3 Reports of human pharmacokinetic (PK) Studies

5.3.3.1 Healthy Subject PK and Initial Tolerability Study Reports

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5.3.5.3 Reports of Analyses of Data from More than One Study

5.3.5.4 Other Study Reports

5.3.6 Reports of Post-marketing experience

5.3.7 Case report forms and individual patient listings

5.4 Literature references