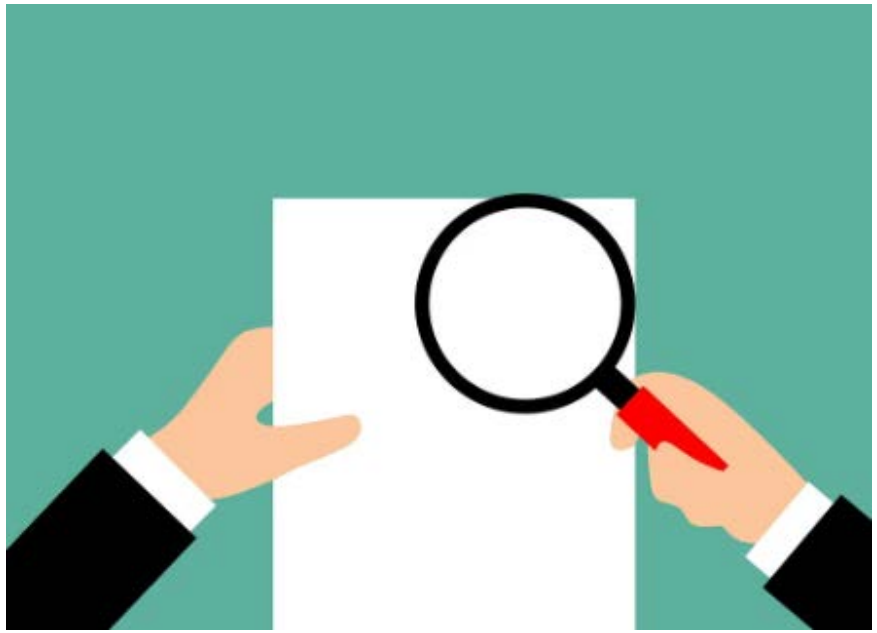
Medicines Control Authority of Zimbabwe



MCAZ assessment of the SmPC

03 OCTOBER 2025

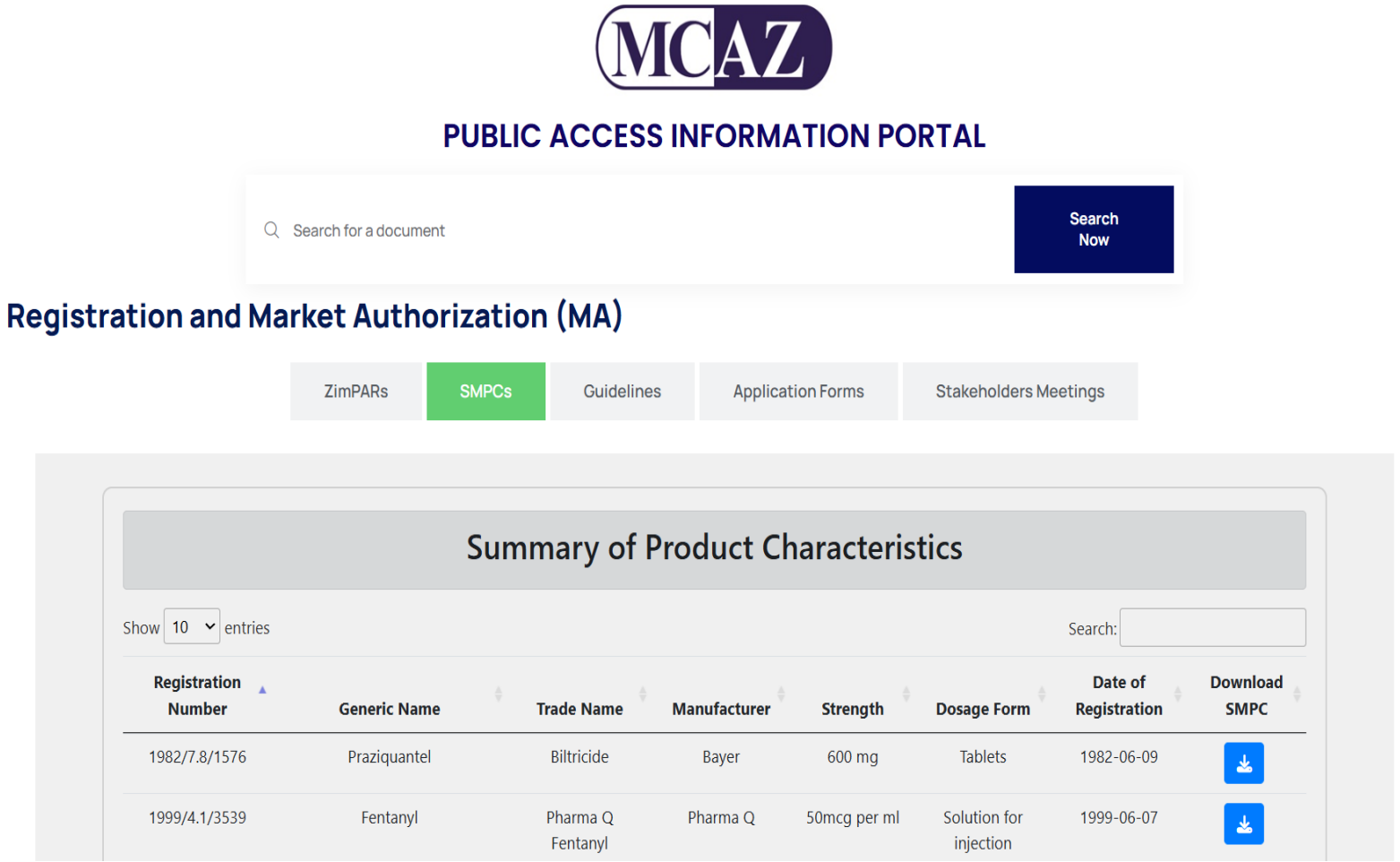
GRACE RURAMAI MATIMBA: CHIEF REGULATORY OFFICER: EVALUATIONS

Outline

1. Importance the SmPC
2. Processing the SmPC
3. Training Purpose

Importance of the SmPC

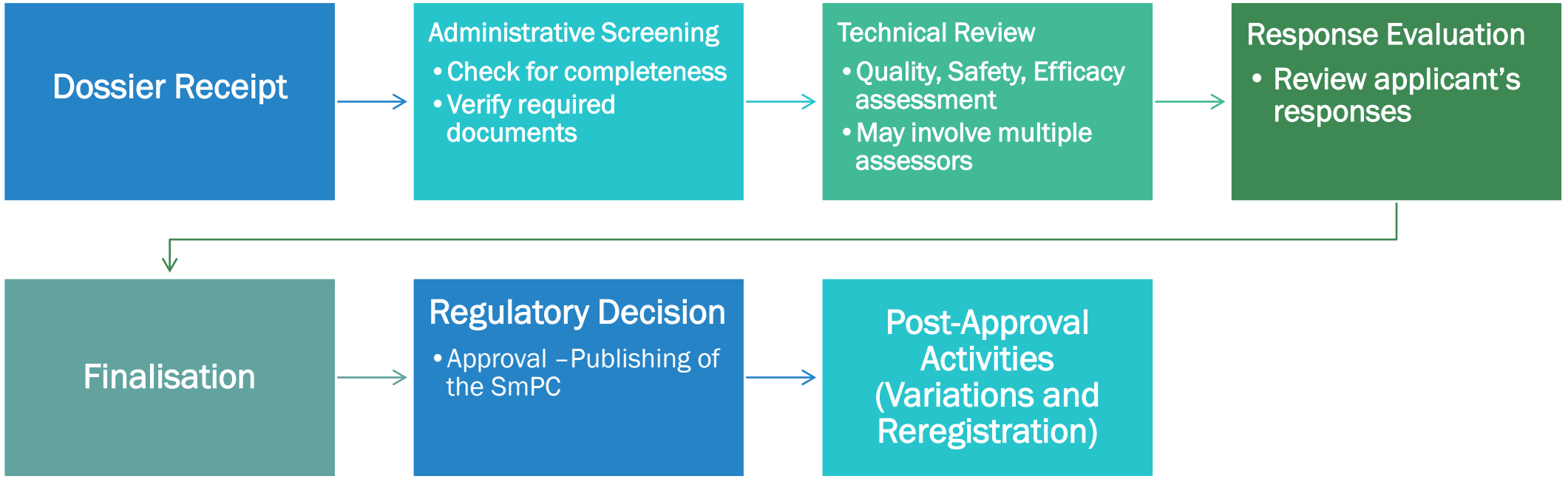
- **Not just a document** - a definitive source of truth for safe and effective use
- Derived from the dossier
- Comprises of Quality, Efficacy, Safety and Administrative information
- Published on MCAZ website https://portal.mcaz.co.zw/re-registration-and-market-authorization-ma/



Journey to publishing of SmPCs

- Transparency
- Provision of information to health professionals and the public
- WHO GBT ML3 indicator
- MCAZ circular 10 of 2022: Publication of Public Assessment Reports and Summary of Product Characteristics for Registered Medicines

The Process


Dossier Receipt
Administrative Screening
• Check for completeness
• Verify required documents
Technical Review
• Quality, Safety, Efficacy assessment
• May involve multiple assessors
Response Evaluation
• Review applicant's responses
Finalisation
Regulatory Decision
• Approval –Publishing of the SmPC
Post-Approval Activities (Variations and Reregistration)

Training Purpose

- Efficiency - Meeting 9-month MCAZ timeline for finalisation
- Resource optmisation (**Reduced Administrative Burden - MCAZ and Lower costs – Industry)**
- Faster approval, quicker time-to-market
- **Promote public health**

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Protecting your right to quality medicines and medical devices

Medicines Control Authority of Zimbabwe

INTRODUCTION TO SmPC

Presented by: Takudzwa Lee Joseph

Date: 02/10/2025

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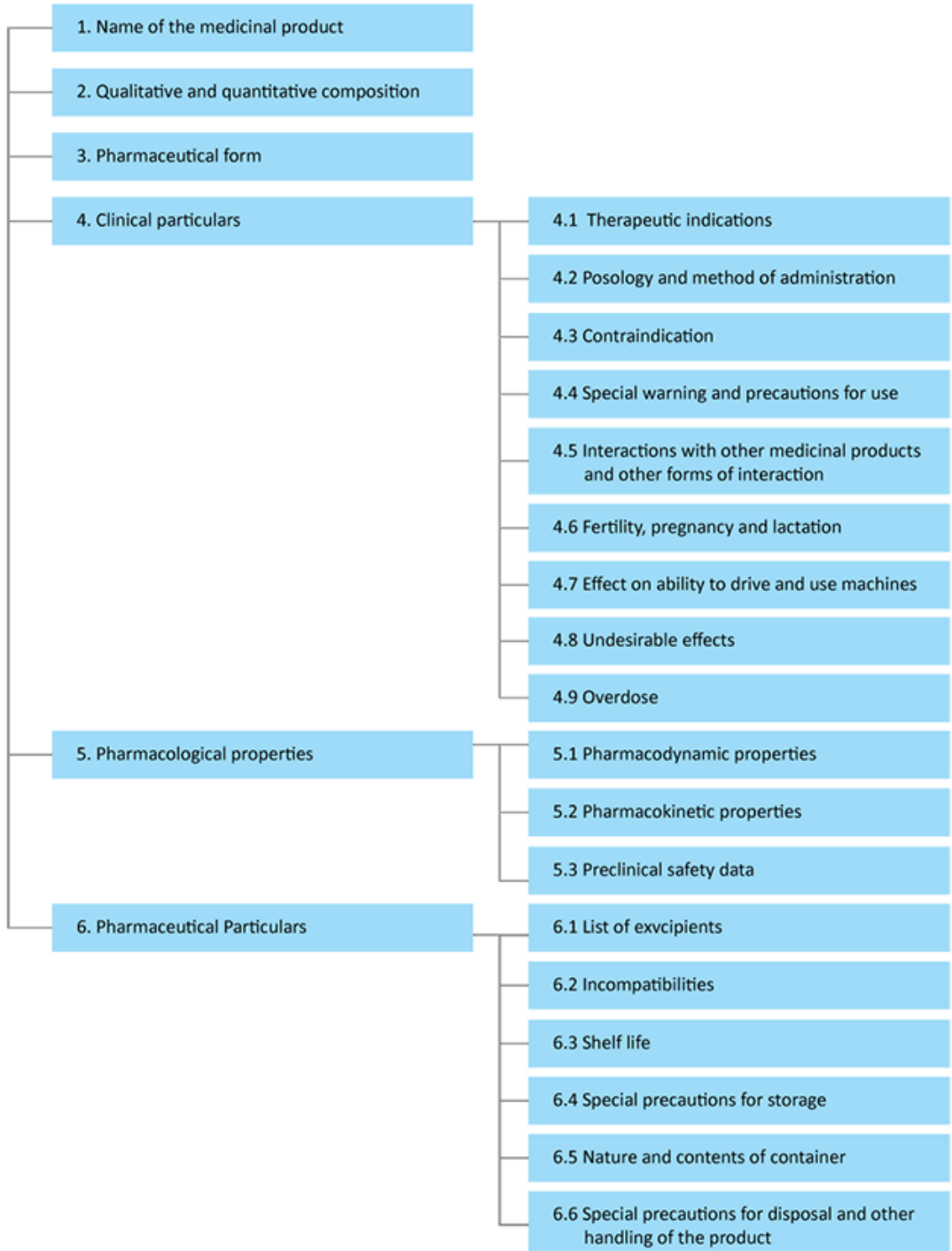
What is a Summary of Product Characteristics (SmPC)?

- A detailed regulatory document summarizing essential information about a medicinal product.
- Supports safe and effective use of medicines.
- It is approved as part of the marketing authorization process and serves as the primary source of information for healthcare professionals on how to use the medicine safely and effectively, including product's composition, indications, dosage, administration, contraindications, warnings, interactions, and pharmacological properties pertaining to all registered products.

Presentation of information in the SmPC

1 Name of medicinal product
2 Qualitative and Quantitative composition
3 Pharmaceutical form
4 Clinical particulars
5 Pharmacological Properties
6 Pharmaceutical particulars
7 Applicant
8 Manufacturer(s)
9 Registration details
10 Date of revision of the text


1. Name of the medicinal product
2. Qualitative and quantitative composition
3. Pharmaceutical form
4. Clinical particulars
4.1 Therapeutic indications
4.2 Posology and method of administration
4.3 Contraindication
4.4 Special warning and precautions for use
4.5 Interactions with other medicinal products and other forms of interaction
4.6 Fertility, pregnancy and lactation
4.7 Effect on ability to drive and use machines
4.8 Undesirable effects
4.9 Overdose
5. Pharmacological properties
5.1 Pharmacodynamic properties
5.2 Pharmacokinetic properties
5.3 Preclinical safety data
6. Pharmaceutical Particulars
6.1 List of exvcipients
6.2 Incompatibilities
6.3 Shelf life
6.4 Special precautions for storage
6.5 Nature and contents of container
6.6 Special precautions for disposal and other handling of the product

Product specific information

- Section 7 to Section 10
- The registration details of the medicinal product.

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SMPC REGULATORY REQUIREMENTS

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Applicant responsibilities

- Drafting the Summary of Product Characteristics of the innovator or similar to the information given in the SmPC of the innovator product for the generic product.
- Include all relevant categories such as clinical pharmacology, indications, contraindications, dosage and administration, overdose, warning and precautions, drug interactions, fertility, pregnancy and lactation, side effects, storage instructions, shelf-life, and mode of use, etc.
- Update information accordingly.
- Submission in **MS Word format** in the **Times New Roman font, font size 12**, page numbers ***(Page 1 of …)*** in Module 1.3.

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MCAZ Responsibilities

- SmPC assessment.
    - In line with information provided in the dossier.
    - Clear and concise language.
- SmPCs must be approved at registration.
- Published on the MCAZ website (portal.mcaz.co.zw), after registration.

DEFINITIONS

- *An innovator medicine* — also called a reference medicine

An original, first-to-market product containing a specific active pharmaceutical ingredient (API) that has been developed and approved based on a full package of quality, safety, and efficacy data.

- *Generic medicine*

A generic medicine is a medicine that is developed to be the same as a medicine that has already been authorised, called the “reference medicine”.

- *Biosimilar*

A similar biological or 'biosimilar' medicine is a biological medicine that is similar to another biological medicine that has already been authorised for use.

General principles

THE CONTENT

- A generic's SmPC should be in all relevant aspects consistent with that of the reference medicinal product.
- The SmPC for a biosimilar medicinal product has to be consistent with the reference medicinal product for the common information applicable to the biosimilar product.
- The indications applied for by the generic/biosimilar applicant should be reflected in section 4.1 of the SmPC as per the indication of the reference medicinal product of the same strength and pharmaceutical form.
- **Any differences of the proposed SmPC vis-à-vis the SmPC of the reference medicinal product should be discussed and justified.**

General principles

TRANSLATIONS

- The corresponding translations from the reference medicinal product's product information must be used, in order to avoid unnecessary linguistic review exercise.
- Obvious translation mistakes in the reference medicinal product's product information should be corrected.

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Formatting considerations

- MCAZ format
- Microsoft Word (MS Word)
- The grammar and spelling should be immaculate.
- Font Type: Times New Roman
- Font size: Twelve (12)
- Pages enumerated as “page 1 of x”, in the footer of each page

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THANK YOU

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References;

MCAZ Guideline on Drafting and Publishing SmPCs
https://portal.mcaz.co.zw/wp-content/uploads/2025/08/MCAZ-EVR-GL-11-Rev-0_July-2025-Guideline-on-SMPcs.pdf

MCAZ Information portal
https://portal.mcaz.co.zw/re-registration-and-market-authorization-ma/

EMA SmPC guideline
https://ec.europa.eu/health/files/eudralex/vol-2/c/smpc_guideline_rev2_en.pdf

European Medicines Agency
https://www.ema.europa.eu/

Annex of the European Commission guideline for excipients
all-languages-annex-european-commission-guideline-excipients-labelling-package-leaflet-medicinal-products-human-use-sante-2017-11668-revision-4_en.xlsx

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SMPC STRUCTURE AND CONTENT

Presented by: Tinashe Hove
Regulatory Officer

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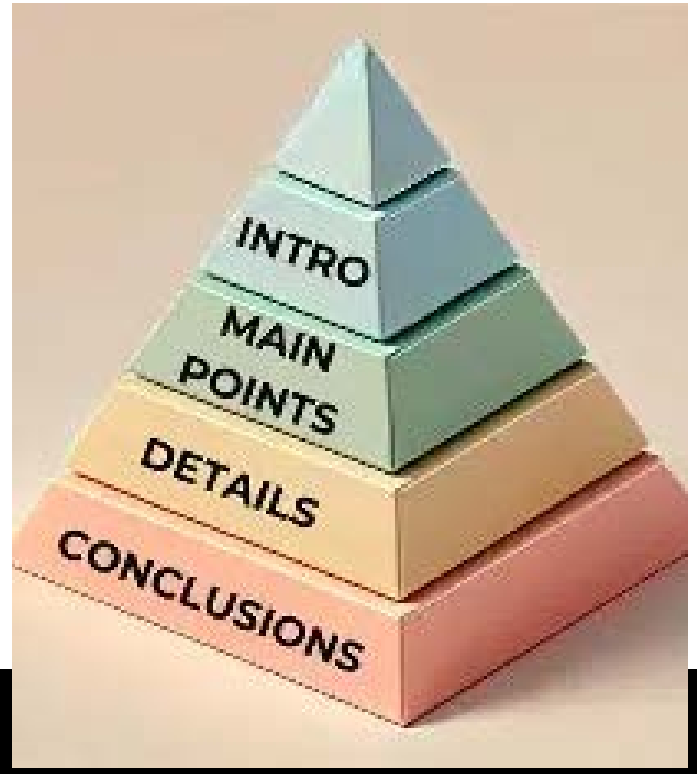
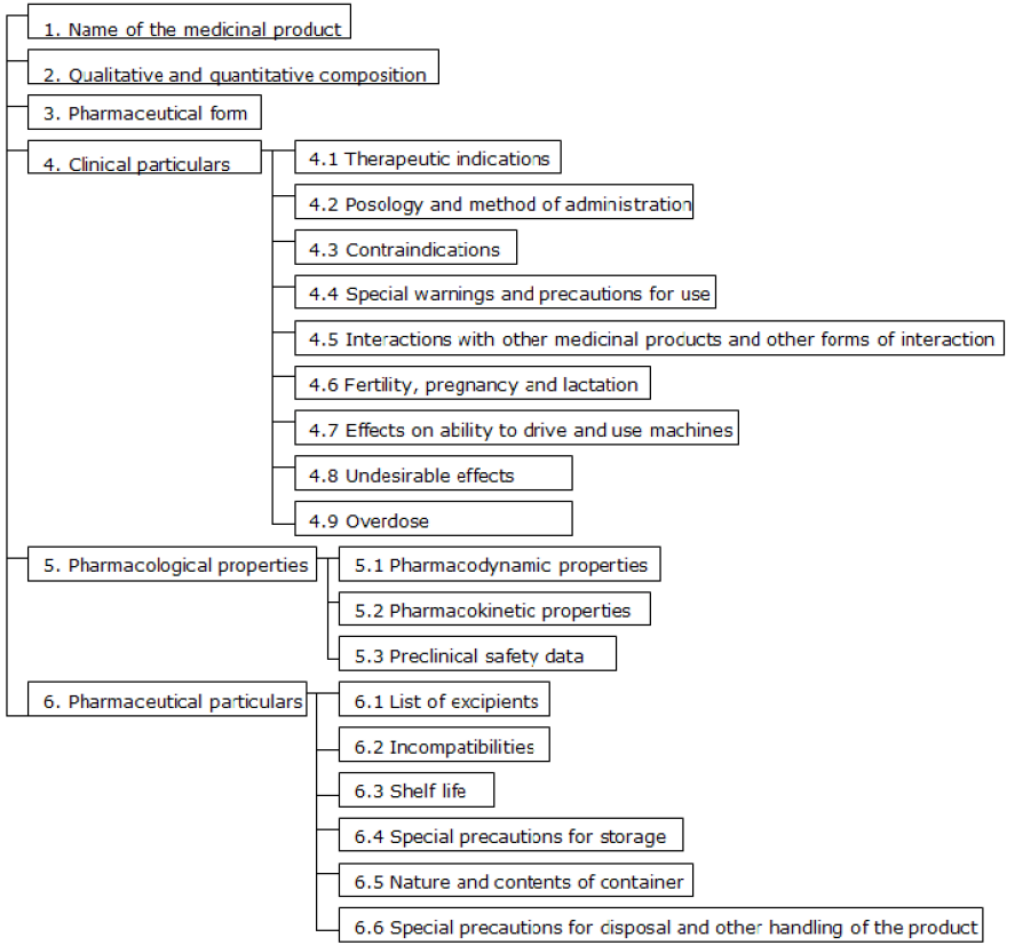
OBJECTIVES

- Sections of the SmPC
- Content of each section
- Product specific sections



SMPC STRUCTURE



SMPC STRUCTURE

- 7 Applicant
- 8 Manufacturer(s)
- 9 Registration details
- 10 Date of revision of the text

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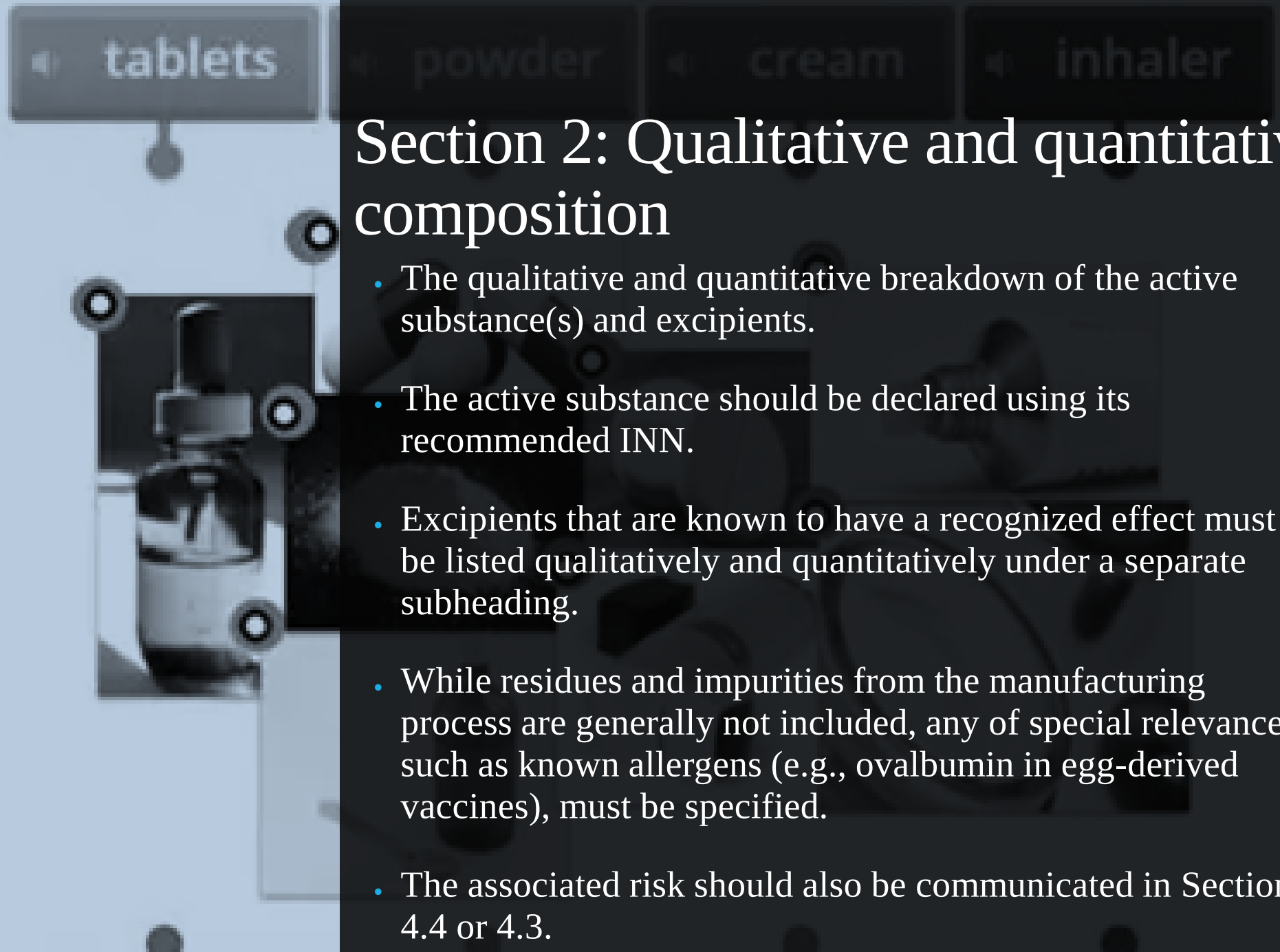
Section 1: Name of medicinal product

The strength and pharmaceutical form should be consistent with the details provided in Section 2 (Qualitative and Quantitative Composition) and Section 4.2 (Posology).

When referring to the active substance itself rather than the product, the International Non-proprietary Name (INN) should be used throughout the SmPC text.



Section 2: Qualitative and quantitative composition

- The qualitative and quantitative breakdown of the active substance(s) and excipients.
- The active substance should be declared using its recommended INN.
- Excipients that are known to have a recognized effect must be listed qualitatively and quantitatively under a separate subheading.
- While residues and impurities from the manufacturing process are generally not included, any of special relevance, such as known allergens (e.g., ovalbumin in egg-derived vaccines), must be specified.
- The associated risk should also be communicated in Section 4.4 or 4.3.

Section 3: Pharmaceutical form

- In singular form and includes a visual description.
- This term should be identical to the one used in Section 1.
- For tablets with a score line
  A. The scoreline line is to facilitate swallowing / for ease of swallowing.
  B. The scoreline allows the tablet to be divided into equal doses.
- The appearance of the product before reconstitution (e.g., a white powder) should be included here, while the appearance after reconstitution should be described in Section 4.2 and 6.6.

Section 4.1: Therapeutic indications

- **Defines the specific**

1. Disease or condition e.g., symptomatic, curative, preventative, or diagnostic treatment.

- well recognised in clinical practice.

2. Target population e.g., specifying age groups or genotype.

- well defined and recognised in clinical practice.
- e.g. age, gender, certain severity stages of the disease, organ function impairment, pharmacogenomics variants.

3. The benefit/risk balance is established to be positive.

- monotherapy/combination therapy.

- use in combinations with other products will result in a negative benefit/risk balance due to safety concerns or uncertainties with respect to the efficacy in combination therapy.

4. Mandatory condition of product usage

- (e.g. concomitant dietary measures, lifestyle changes or specific screening modalities).

Section 4.2: Posology and Method of Administration

- Dosage for each indication
  i. including the dose
  ii. dosing interval
  iii. duration of treatment.
- The method of administration.
- Special populations e.g children and adult populations, dosage information must be based on clinical data and clearly outline the recommended dose.

Section 4.3 : Contra-indications

- **Situations where the medicine must not be given for safety reasons.**
- Lack of data alone should not lead to a contraindication.
- The most common contraindication is hypersensitivity to the active substance or excipients14. If hypersensitivity is a contraindication, it should always be included in the SmPC, except in exceptional circumstances where the benefit of the drug outweighs the risk.

Section 4.4: Special Warnings and Precautions for Use

- **Information on specific risks that require a healthcare professional to be warned or to take precautions to avoid harm.**
    1. Conditions to be fulfilled before use.
    2. Serious adverse reactions that require alerting healthcare professionals.
    3. Risks associated with starting or stopping the product.
    4. Special populations that are at increased risk.

Section 4.5: Interaction with Other Medicinal Products and Other Forms of Interaction

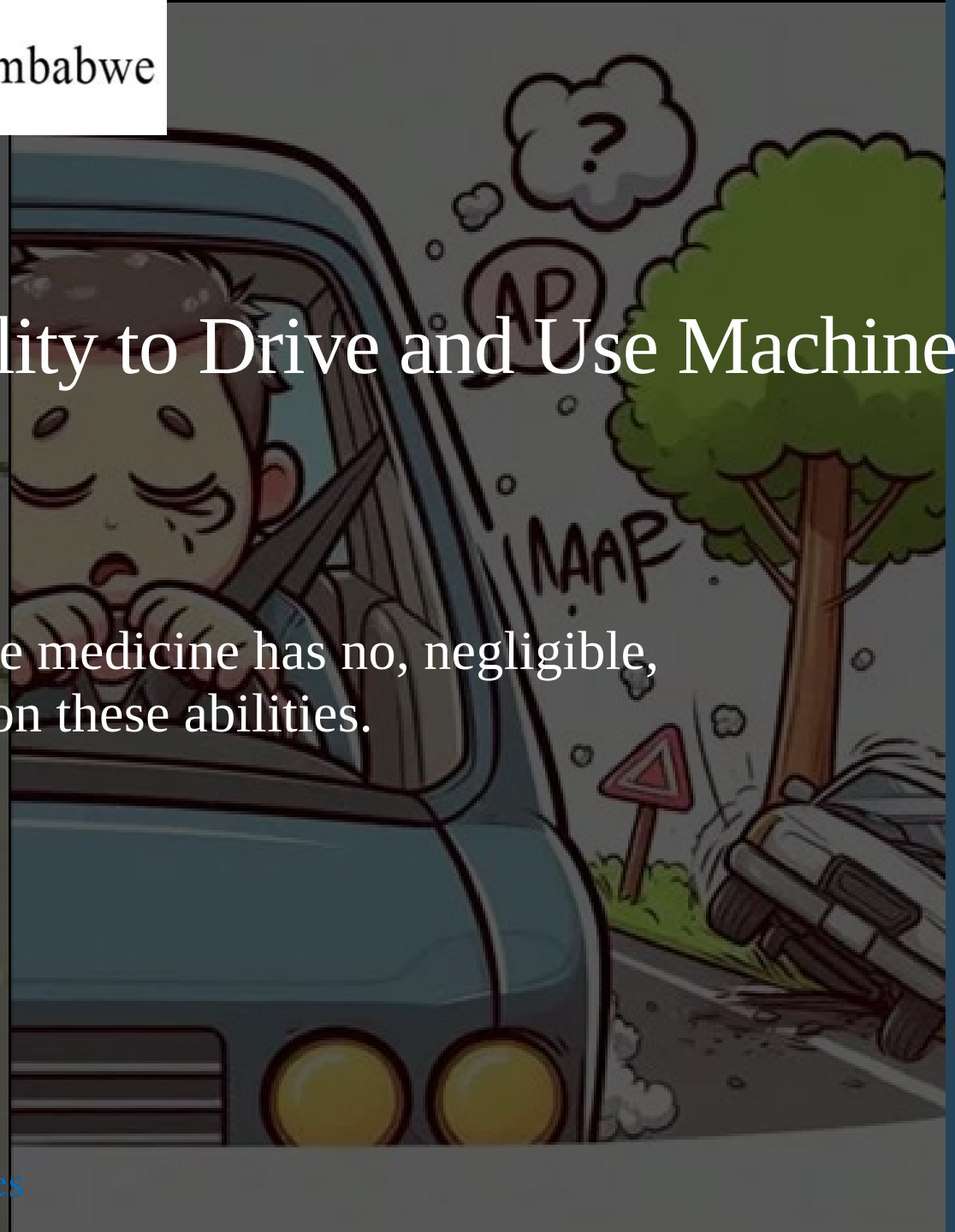
- Potential clinically relevant interactions based on the medicine's pharmacodynamic and pharmacokinetic properties.
- Recommendations may include contraindications, warnings against concomitant use, or precautions such as dose adjustments.
- The information should be structured to highlight clinically relevant interactions that result in a recommendation for the use of the medicine or other medicines.

Section 4.6: Fertility, Pregnancy and Lactation

- Medicine's use in relation to reproduction, including fertility, pregnancy, breastfeeding, and the health of the foetus, child, and mother.
- Recommendations should be practical, based on all available data from non-clinical studies, clinical data, and therapeutic practice.
- Efforts should be made to update these recommendations as human experience with exposed pregnancies becomes available.

Section 4.7: Effects on Ability to Drive and Use Machines

The SmPC should specify whether the medicine has no, negligible, minor, moderate, or major influence on these abilities.



Section 4.8: Undesirable Effects

- All adverse reactions for which a causal relationship with the medicinal product is at least a reasonable possibility.

  [clinical trials, post-authorization safety studies, and spontaneous reporting]

- Summary of the safety profile.
- List of adverse reactions by frequency and a description of selected adverse reactions.

Section 4.9: Overdose

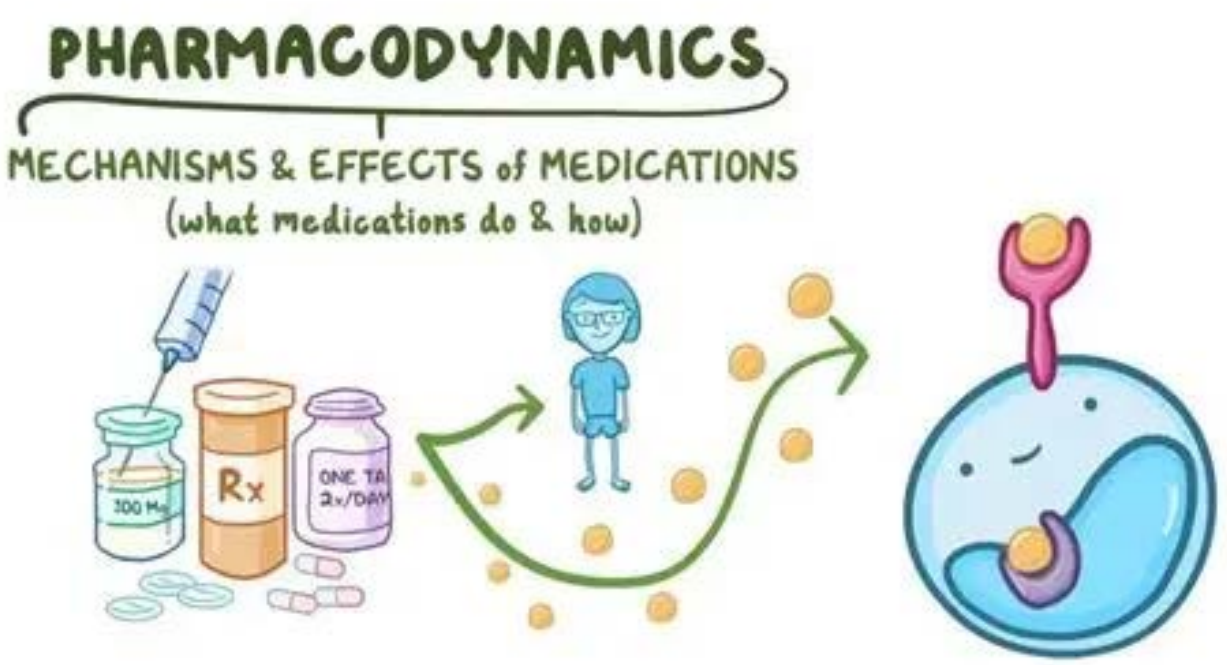
Detection and management of an overdose.

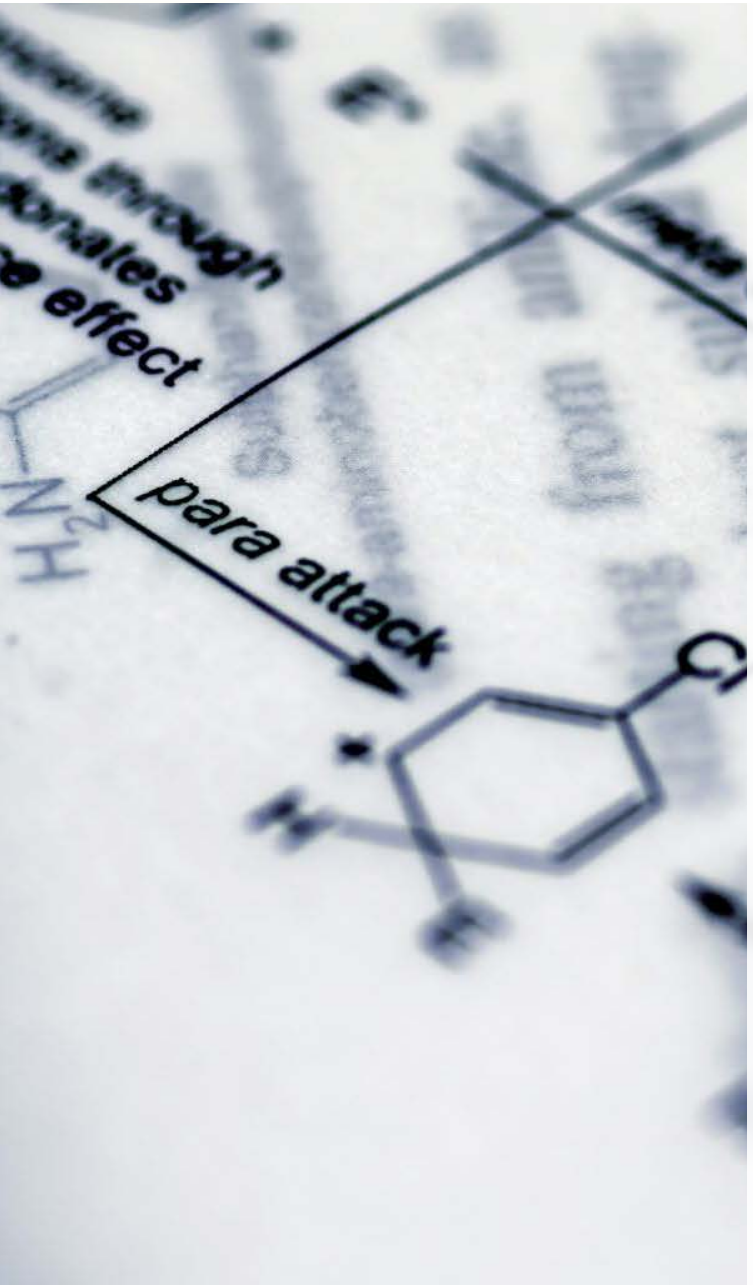
- Acute symptoms, signs, and potential after-effects of different dose levels based on all available information.
- Signs and symptoms expected based on the observed clinical safety profile and experience with similar compounds, if no cases of overdose have been reported.
- management of overdose, including monitoring, the use of an antidote, or methods to increase elimination

Section 5.1: Pharmacodynamic properties

Relevant to healthcare professionals on the approved therapeutic indications and clinical safety data, including information on special populations.

- Pharmacological classification
- Mechanism of action
- Clinical efficacy and safety





Section 5.2: Pharmacokinetic properties

- Active substance(s) absorbed, distributed, metabolized, and eliminated from the body.
- Relevant to the advised dose, strength, and pharmaceutical formulation.
- Difference in specific groups of patients.

Note: If a new formulation has significant pharmacokinetic differences, a warning or precaution should be included in Section 4.2 or 4.4, with supporting data in Section 5.2.

Section 5.3: Preclinical safety data

Non-clinical testing that could be relevant to the prescriber.

- Brief description of any findings from toxicology, genotoxicity, carcinogenicity, or reproduction and development studies.
- If a potential risk to the environment has been identified, it should also be included in this section.

Section 6: Pharmaceutical particulars

- **Section 6.1 (List of excipients),** including those present in small amounts and ingredients of printing inks, should be listed.
- **Section 6.2 (Incompatibilities):** Any known physical or chemical incompatibilities.
- **Section 6.3 (Shelf life):** The shelf life of the unopened product, as well as the shelf life after the first opening, reconstitution, or dilution, should be specified.
- **Section 6.4 (Special precautions for storage):** Any specific storage conditions, such as temperature or protection from light.
- **Section 6.5 (Nature and contents of container):** The primary packaging and any accessory devices provided.
- **Section 6.6 (Special precautions for disposal and other handling):** This section includes instructions for the preparation, handling, and disposal of the medicinal product. It also addresses any specific handling precautions for the healthcare professional, such as the use of a needle safety system.

Product specific details

- **Section 7 - Applicant**
  Full name and address
- **Section 8 - Manufacturer(s)**
  Full name and address
- **Section 9 - Registration details**
  Zimbabwe registration number:
  Category for distribution:
- **Section 10 - Date of revision of the text**
  Month and Year

References

MCAZ Guideline on Drafting and Publishing SmPCs
https://portal.mcaz.co.zw/wp-content/uploads/2025/08/MCAZ-EVR-GL-11-Rev-0_July-2025-Guideline-on-SMPcs.pdf

MCAZ Information portal
https://portal.mcaz.co.zw/re-registration-and-market-authorization-ma/

WHO medicines guidance
https://extranet.who.int/prequal/medicines/who-medicines-prequalification-guidance

EMA SmPC guideline
https://ec.europa.eu/health/files/eudralex/vol-2/c/smpc_guideline_rev2_en.pdf

Information on benefit-risk of medicines: patients', consumers' and healthcare professionals' expectations
https://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/12/WC500018433.pdf

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Medicines Control Authority of Zimbabwe

SMPCs for FIXED DOSE COMBINATION (FDCs) MEDICINAL PRODUCTS

M. F. Nyamukapa

MCAZ Medicines Control Authority of Zimbabwe

Fixed Dose Combination medicinal products

Definition: **The combination of active substances within a single pharmaceutical form of administration**.

The product information should be an **integrated** evaluation of the FDC, and not a summation of the product information for each of the actives.

Section 1: Name of the medicinal product

- The actives should be followed by the strengths, the pharmaceutical form.

  e.g. Active A/Active B/Active C 100mg/ 5mg/ 50mg tablets.

  Trade name – DEFGHI

Section 4.1 Therapeutic indications

- The presence of each active substance makes a contribution to the claimed effect or improves the overall benefit risk ratio by mitigating side effects.
- A first line, second line or substitution indication.

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X is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral treatment-naïve or are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in X.

Treatment of essential hypertension. This fixed dose combination is indicated in patients whose blood pressure is not adequately controlled by X alone or Y alone.

Treatment of essential hypertension as substitution therapy in adult patients whose blood pressure is adequately controlled on the combination of amlodipine, valsartan and hydrochlorothiazide (HCT), taken either as three single-component formulations or as a dual-component and a single-component formulation.

Examples of Indications

Section 4.2 Posology and method of administration

- The product should be formulated so that the dose and proportion of each substance present is appropriate for the intended use.
- If the strength(s) is (are) not suitable to adjust the posology to a special population subgroup (e.g. patient with renal impairment), it should be stated in section 4.2.

X is not recommended for patients with moderate or severe renal impairment (creatinine clearance < 50 ml/min). Patients with moderate or severe renal impairment require a dose interval adjustment of A and B that cannot be achieved with the combination tablet.

Section 4.3 and Section 4.4 Contraindications, Warnings and precautions for use

Inform on additive (or counteractive) effect of the different components.

Inform on the component(s) leading to the warning or precaution when known and specific to one of the components.

Presentation of the order of warnings and precautions should in principle be determined by the importance of the safety information provided

– All contraindications can be listed together.

– Warning and precautions should be integrated and presented with sub-headings naming the effect or the sub-population at risk to facilitate usability.

Section 4.5: Interactions with other medicinal products

No drug interaction studies have been performed using X. As X contains efavirenz, emtricitabine and tenofovir disoproxil fumarate, any interactions that have been identified with these agents individually may occur with X.

Y contains lamivudine and zidovudine, therefore any interactions identified for these individually are relevant to Y. Clinical studies have shown that there are no clinically significant interactions between lamivudine and zidovudine.

Zidovudine is primarily metabolised by UGT enzymes; co-administration of inducers or inhibitors of UGT enzymes could alter zidovudine exposure. Lamivudine is cleared renally. Active renal secretion of lamivudine in the urine is mediated through organic cation transporters (OCTs); co-administration of lamivudine with OCT inhibitors or nephrotoxic drugs may increase lamivudine exposure.

Section 4.6 Fertility, pregnancy and lactation

- Clinical data and relevant conclusions from non-clinical toxicity studies—if available—for both the fixed combination and each individual component should be summarised before making recommendations on use.
- Recommendations should be based on an integrated evaluation of the FDC.

Breast-feeding
No studies in lactating animals have been conducted with the combined active substances of X. In studies performed with the individual active substances, both sitagliptin and metformin are excreted in the milk of lactating rats. Metformin is excreted in human milk in small amounts. It is not known whether sitagliptin is excreted in human milk. X must therefore not be used in women who are breast-feeding (see section 4.3).

Section 4.8 Undesirable effects

- All safety data from the fixed dose combination and the individual components should be considered.
- Summary of safety profile - most serious and most frequent adverse reactions of the fixed combination, based on the integrated evaluation of all relevant safety data.
- All adverse reactions should be listed in a single tabulated listing with its respective frequency category for the fixed combination.
- In subsection c, under the description of selected adverse reactions, where known, information should indicate which adverse reactions are typically attributable to which active substances. This can also highlight any clinically relevant differences in the safety profile of the combination compared to the individual components.

Examples

Summary of safety profile

The most frequently reported adverse reactions with X are dyskinesias occurring in approximately 19% of patients; gastrointestinal symptoms including nausea and diarrhoea occurring in approximately 15% and 12% of patients, respectively; muscle, musculoskeletal and connective tissue pain occurring in approximately 12% of patients; and harmless reddish-brown discolouration of urine (chromaturia) occurring in approximately 10% of patients. Serious events of gastrointestinal haemorrhage (uncommon) and angioedema (rare) have been identified from the clinical trials with X or entacapone combined with levodopa/DDC inhibitor. Serious hepatitis with mainly cholestatic features, rhabdomyolysis and neuroleptic malignant syndrome may occur with X although no cases have been identified from the clinical trial data.

Tabulated listing of adverse reactions

Vascular disorders	
Common	Orthostatic hypotension[h]
Uncommon	Hypotension[c, a]
Respiratory, thoracic and mediastinal disorders	
Uncommon	Cough[a]
Very rare	Respiratory distress (including pneumonitis and pulmonary oedema)[h]
Gastrointestinal disorders	
Common	Diarrhoea[c, a, h], decreased appetite[h], mild nausea and vomiting[h]
Rare	Abdominal discomfort[h], constipation[h]
Very rare	Pancreatitis[h]

[c] – Adverse reaction observed with X (aliskiren + hydrochlorothiazide)
[a] – Adverse reaction observed with monotherapy with aliskiren
[h] – Adverse reaction observed with monotherapy with hydrochlorothiazide

Section 5.1: Pharmacodynamic properties

- The mechanism of action of each component should be presented.
- Unless limited to the simplification of the administration, the **rationale** of the fixed combination should be explained. (e.g. potentiation or counteracting effect)
- Results of clinical trials supporting the indication(s) and recommended posology for the use of the products in combination may be presented.

Section 5.2: Pharmacokinetic properties

- Pharmacokinetic information on the fixed-dose combination—such as the rate and extent of absorption of each component compared to when they are administered individually—should be presented first.
- This should be followed by a description of the pharmacokinetic properties of each individual component.

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References

MCAZ Guideline on Drafting and Publishing SmPCs
https://portal.mcaz.co.zw/wp-content/uploads/2025/08/MCAZ-CVR-GL-11-Rev-0_July-2025-Guideline-on-SMPCs.pdf

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SmPC of fixed combination medicinal products
https://www.ema.europa.eu/en/documents/presentation/presentation-summary-product-characteristics-fixed-combination-medicinal-products_en.pdf

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