SUMMARY OF PRODUCT CHARACTERISTICS GUIDELINES

(CTD Module 1.5.14)

Document History: **1st Edition**

Effective Date:

Drug Regulatory Authority of Pakistan
Islamabad - Pakistan.

HISTORY

This is the first edition of these guidelines.

APPLICATION - Guideline for Industry

This document is applicable to the firms who intends to apply for registration / Marketing Authorization of human drug product.

PURPOSE

This guideline is intended to provide supportive information for preparation of summary of product characteristics (SmPC) for registration / market authorization of pharmaceutical and biological products of all types including New drug product, Generic drug product and biosimilar drug product for import, export or local manufacturing. This guideline provides advice on the principles of presenting information in the SmPC.

BACKGROUND

Section 7 (c) (ix) of DRAP Act 2012, mandated the systematic implementation of internationally recognized standards of World Health Organization, International Conference on Harmonization (ICH), and Food and Drug Administration guidelines etc.

In this context, Registration Board in various meetings has deliberated the contents of summary of Product Characteristics for pharmaceutical and biological drug products. This document transforms the decisions and advices of Registration Board into a guidance document for preparation of summary of Product Characteristics with application dossier submission in the CTD module.

These guidelines conform to Drugs Act 1976 and rues framed there under and some parts such as classification, definitions, and description etc., have been adopted from WHO guidelines on registration / market authorization procedures.

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INTRODUCTION

The Summary of Product characteristics (SmPC) is the basis of information for healthcare professionals for use of drug product ensuring its quality, safety and efficacy. It also provides a basis for preparation of medicine package leaflet. The Patient information Leaflet (PiL) shall be drawn up in accordance with the SmPC. It describes the set of characteristics of the drug product as distilled by the assessment process. The SmPC also sets the limit for advertising and promotion in terms of indications and claims on the drug product to healthcare professionals. SmPC is an alive document that will be updated as new data emerges related to the safety or efficacy of drug product. The registration / market authorization holder shall supply any new information without delay which may require the variation of the marketing authorisation / registration including the revision of SmPC.

LEGAL PROVISIONS RELATED TO SmPC

Rule 26 of the Drugs (Licensing, Registering and Advertising) Rules, 1976, as amended vide S.R.O 713(I)/2018 dated 8th June, 2018, under 26(1) section 1.5.14 requires that in order to obtain registration/marketing authorization of drug product, a Summary of Product Characteristics (SmPC) is required to be included in the application dossier. The SmPC is the part of drug registration / marketing authorization and it can only be changed with the approval of Registration Board.

GENERAL CONSIDERATIONS

Applicants are advised to submit a separate SmPC for each finished drug product in prescribed format provided as Annexure-I in this document, under Module 1.5.14 as Summary of Product Characteristics (SmPC).

The Applicant shall maintain the integrity of each section of the document by only including information in each section which is relevant to the section heading. However, some issues may need to be addressed in more than one section of the SmPC and in such situations the individual statements may cross-refer to other sections when these contain relevant additional information.

Applicants are advised to use MedDRA for consistency and standardization of medical terminology throughout the SmPC, particularly for describing ADRs, Undesirable effects and contraindication, etc.

The following information is required to be submitted under Module 1.5.14 as Summary of Product Characteristics (SmPC):-

1. NAME OF THE MEDICINAL PRODUCT

Provide the { Proprietary / brand } name followed by the strength and pharmaceutical form for product to be marketed. However, for the purpose of referring the product in the SmPC text, the strength and pharmaceutical dosage form of product is not required to be mentioned with name. Whereas, International Non-proprietary Name (INN) or the usual common name of the active pharmaceutical ingredients / drug substance should be used when referring to properties of the drug substance(s) rather than those of the product. The use of pronouns (e.g. "it") is encouraged for referring the product, whenever possible.

1.1. Strength

Strength shall be mentioned with the relevant quantity in a consistent manner with the quantitative composition and posology.

i. State different strengths of same product in the same way i.e. 100mg, 250mg, 750mg.
ii. Avoid use of decimal points where can be easily removed, for example state 250microgram instead of 0.25mg).
iii. Use same unit for range of drug product of the same pharmaceutical dosage form to maintain comparability like 0.25mg, 1mg and 6mg is more appropriate rather 250 microgram, 1 mg and 6 mg.
iv. When micrograms and millions are used as unit, it is recommended to spell out units in full form rather using abbreviation for safety reasons.

1.2. Pharmaceutical form

Pharmaceutical dosage form of drug product shall be mentioned using single full Standard Term in accordance to Pharmacopoeia in the plural form (e.g. tablets). Route of administration or container shall not be mentioned with pharmaceutical form unless there is a particular safety reason for their inclusion or where there are identical products, which can only be distinguished by reference to the route of administration or to the container.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The qualitative and quantitative composition shall be mentioned in terms of the active pharmaceutical ingredient(s) / Drug Substance(s) and excipients (wherever required, e.g. excipients with known effect and knowledge of which are essential for proper administration of the medicinal product), in accordance to the following standards:-

2.1. Qualitative declaration

Active Pharmaceutical Ingredients / Drug Substance shall be declared using International non-proprietary name (INN)/ Pharmacopoeial name, accompanied by its relevant salt, hydrate form etc.

2.2. Quantitative declaration

The quantity of the drug substance should be expressed per unit volume, or per unit of weight or per dosage unit (for metered dose inhalation products, per delivered dose and/or per metered dose) and should be related to the declaration of strength in the section 1.

2.3. Salts and hydrates

Where the drug substance is present in the form of a salt or hydrate, the quantitative composition should be expressed in terms of the mass of the therapeutically active moiety (base, acid or anhydrous material), e.g. '10 mg atorvastatin (as calcium trihydrate)' or atorvastatin calcium trihydrate equivalent to 10 mg atorvastatin'.

Where a salt is formed *in situ* during the preparation of the finished product (e,g. during the mixture of solvent and powder), the quantity of the active moiety should be stated, with a reference to the in *situ* formation of salt e.g. 5mg of saxagliptin (as hydrochloride).

Where for drug products the strength of Active Pharmaceutical Ingredients / Drug Substance is traditionally expressed in the form of a salt or hydrate, the quantitative composition shall be declared with salt or hydrate, e.g. '500 mg of Metformin hydrochloride or 60mg of diltiazem hydrochloride.

2.4. Esters and pro-drugs

Where the Active Pharmaceutical Ingredient / Drug Substance is an ester or pro-drug, the quantitative composition should be stated in terms of the quantity of the ester or pro-drug.

However, when the active moiety is an Active Pharmaceutical Ingredients / Drug Substance of an already approved drug product, the quantitative composition should also be stated in terms of the quantity of this active moiety (e.g. 75 mg of fosphenytoin is equivalent to 50 mg of phenytoin).

2.5. Oral powders for solution or suspension

The quantity of Active Pharmaceutical Ingredients / Drug Substance should be stated per unit dose if the product is a single-dose preparation or otherwise per unit dose volume after reconstitution.

2.6. Parenterals excluding powders for reconstitution

For single-dose parenterals, where the total contents of the container are given in a single dose ('total use'), the quantity of Active Pharmaceutical Ingredient(s) / Drug Substance(s) should be stated per presentation (e.g. 20 mg etc.) not including any overages or overfill. The quantity per ml and the total labelled volume should also be given.

For single-dose parenterals, where the amount to be given is calculated on the basis of the patient's weight or body surface or other variable ('partial use'), the quantity of Active Pharmaceutical Ingredient(s) / Drug Substance(s) should be stated per ml. The quantity per total labelled volume should also be given. Overages or overfills should not be included.

For multi-dose and large volume parenterals, the quantity of Active Pharmaceutical Ingredient(s) / Drug Substance(s) should be stated per ml, per 100 ml, per 1000 ml, etc. as appropriate, except for multidose vaccines containing 'n' doses of the same dose. In this case, the strength should be expressed per dose volume. Overages or overfills should not be included.

Where appropriate, e.g. for X-ray contrast media, and parenterals containing inorganic salts, the quantity of Active Pharmaceutical Ingredient(s) / Drug Substance(s) should also be indicated in millimoles. For X-ray contrast media with iodine-containing drug substances, the quantity of iodine per ml should be stated in addition to the quantity of the drug substance.

2.7. Powders for reconstitution prior to parenteral administration

When the product is a powder to be reconstituted prior to administration, the total quantity of Active Pharmaceutical Ingredient / Drug Substance in the container should be stated not including overages or overfills, as well as the quantity per ml when reconstituted, unless there are several means of reconstituting, or different quantities used, which result in different final concentrations.

2.8. Concentrates

The quantity should be stated as the content per ml in the concentrate and as the total content of the Active Pharmaceutical Ingredient / Drug Substance. The content per ml when diluted as recommended should also be included unless the concentrate is to be diluted to, within a range of different final concentrations.

2.9. Transdermal patches

The following quantitative details should be given: the content of Active Pharmaceutical Ingredient / Drug Substance per patch, the mean dose delivered per unit time, and the area of the releasing surface, e.g. 'Each transdermal patch contains 7.5 milligram of fentanyl in a patch size of 30 cm^2, releasing a 75 micrograms of fentanyl per hours'.

2.10. Multidose solid or semi-solid products

Quantity of Active Pharmaceutical Ingredient(s) / Drug Substance(s) should be stated, where possible, per unit dose, otherwise per gram, per 100 g or percentage, as appropriate.

2.11. Biological medicinal products

Expression of strength.
The quantity of biological medicinal products should be expressed in terms of mass units, units of biological activity, or International Units as appropriate for the particular product.

The biological origin of the active substance.
The origin of the active substance/ drug substance should be defined briefly. Thus, the nature of any cellular system(s) used for production and, if relevant, the use of recombinant DNA technology should be specified. The entry should take the form: "produced in XXX cells <by recombinant DNA technology>".
The following are examples of the application of this principle:

"produced in human diploid (MRC-5) cells",
"produced in Escherichia coli cells by recombinant DNA technology",
"produced in chick-embryo cells",
"produced from the plasma of human donors",

Special provisions for normal immunoglobulins.
In case of normal immunoglobulins, the IgG subclass distribution should be stated in terms of percent of total IgG present. The upper limit of the IgA content should follow.

Special provisions for vaccines.

In case of vaccines, the content of drug substance per dose unit (e.g. per 0.5 ml) should be stated. Adjuvants, if present, should be stated qualitatively and quantitatively. Residues that are of special relevance (e.g. ovalbumin in egg derived vaccines) should be specified.

3. PHARMACEUTICAL FORM

The pharmaceutical dosage form should be described by a full standard pharmacopeial term by using the singular form. The term used in this section should be the same as the term used in section 1.

A visual description of the appearance of the product (colour, markings, etc.) should be given, in a separate paragraph to the standard term, including information on the actual size of a solid oral formulation, e.g.'Tablet White, circular flat bevelled-edge tablets of 5 mm marked '100' on one side'. Example is confusing.

In case of tablets designed with a score line, information should be given on whether or not reproducible dividing of the tablets has been shown. e.g. 'the scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses', 'the tablet can be divided into equal halves'.

Similarly, Information on pH and osmolarity should be provided, as appropriate. In case of products to be reconstituted before use, the appearance before reconstitution should be stated in this section. Appearance of the product after reconstitution should be stated in sections 4.2 and 6.6.

4. CLINICAL PARTICULARS

The following contents of the summary of product characteristics (SmPC) should be in all relevant aspects consistent with the current version of the reference medicinal product as approved by reference regulatory authority. This information should be updated regularly when new information becomes available for reference medical product.

4.1. Therapeutic indications
4.2. Posology and method of administration
4.3. Contraindications
4.4. Special warnings and precautions for use
4.5. Interaction with other medicinal products and other forms of interaction
4.6. Fertility, pregnancy and lactation
4.7. Effects on ability to drive and use machines

4.8. Undesirable effects

4.9. Overdose

5. PHARMACOLOGICAL PROPERTIES

This section shall contain information which is relevant to the prescriber and to other health-care professionals, taking into account the approved therapeutic indication(s) and the potential adverse drug reactions. This information should be updated regularly when new information becomes available for reference medicinal product as approved by any of the reference regulatory authory.

The following contents of the summary of product characteristics (SmPC) shall be consistent with the current version of the reference medicinal product.

5.1. Pharmacodynamics properties

- Pharmacotherapeutic group and ATC code shall be provided:
- Mechanism of action (if known)
- Pharmacodynamic effects
- Clinical Safety and Efficacy

The information related to pediatric population shall be provided in a separate subheading.

5.2. Pharmacokinetic properties

The information related to pharmacokinetic properties of Active Pharmaceutical Ingredient(s) / Drug Substance(s) with regard to dose, strength and pharmaceutical formulation.

5.3. Preclinical safety data

The information related to the non-clinical testing which has relevance to the prescriber, in recognizing the safety profile of the medicinal product shall be presented in this sub section briefly.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

A list should be given of the excipients, expressed qualitatively only. All excipients, which are present in the product, should be included. For transdermal patches, all ingredients of the patch (including the adhesive, release liner and backing film) should be mentioned.

Excipients should be referred to by their recommended INN, if existing, accompanied by the salt or hydrate form, if relevant or by their Pharmacopoeial name. If an excipient has neither an INN nor Pharmacopoeial name, it should be described by its usual common name.

The ingredients in excipient mixtures should be listed individually. In cases where the full composition of a flavour or fragrance is not known to the applicant or is too complex, it may be declared in general terms (e.g. 'orange flavour', 'citrus perfume'). However, any of the components, which are known to have a recognized action or effect, should be included.

Ingredients that may or may not be added for the pH adjustment should be followed by the parenthesis '(for pH-adjustment)'.

For clarity, it is recommended that each excipient be listed on a separate line. It can be useful to list excipients according to the different parts of the product, e.g. tablet core/coat, capsule contents/shells, etc. For products that are presented in more than one container or in dual-chamber containers, the excipients should be listed per container or per chamber.

6.2. Incompatibilities

Information on physical and chemical incompatibilities of the medicinal product with other products with which it is likely to be mixed or co-administered should be stated. This is particularly important for medicinal products to be reconstituted and/or diluted before parenteral administration. Significant interaction problems, e.g. sorption of products or product components to syringes, large volume parenteral containers, tubing, in-line filters, administration sets, etc. should be stated.

6.3. Shelf life

The shelf life should be given for the finished drug product as packaged (primary and secondary) for sale and, if appropriate, after dilution or reconstitution or after first opening.

A clear statement of the shelf life should be given, in an appropriate unit of time. The information should always be based upon the stability data as per applicable conditions.

An in-use shelf life may need to be stated for some drug products if development studies have found it to be necessary. If a product can be used by preparing different concentrations, e.g. for use in children, the physicochemical stability throughout the entire concentration range shall be stated; e.g. "The stability has been demonstrated between x mg/ml and y mg/ml for t hours/days at 30 ºC and 2-8 ºC, as appropriate".

In case there are different shelf lives for different containers closure system, reference should be made to the respective container closure system.

When a device is supplied together with a medicinal product, the in-use shelf-life of the device should be given, where applicable.

6.4. Special precautions for storage

Storage warnings should be stated using one or more of the standard statements along with an explanation specifying whether the product is sensitive to temperature, light and/or moisture. When a specific storage warning is required, such warning statements should be consistent between the SmPC, Packaging label and Patient information Leaflet (PiL).

For storage of sterile products that have been opened, diluted or reconstituted, a cross-reference should be made to section 6.3.

A warning to keep the product out of the reach and sight of children should be included in the SmPC, Packaging label and Patient information Leaflet (PiL).

6.5. Nature and contents of container

Reference should be made to the immediate container using the Pharmacopoeial standard term; the material of construction of the immediate container should be stated ('glass vials', 'PVC/Aluminium blisters', 'HDPE bottles'); and any other component of the product should be listed, e.g. needles, swabs, measuring spoons, syringes inhaler devices, desiccant. The graduation on measuring devices should be explained. The container of any solvent provided with the drug product should also be described.

Excessive detail, e.g., concerning the colour of the stopper, the nature of the heat-seal lacquer, should usually not be included. For parenteral preparations, when enclosure colour is used to differentiate between the presentations of a product, this should be stated here.

If appropriate, it should be indicated if the container closure is child-resistant.

Examples on the text in this section:
'<Volume> ml suspension in a pre-filled syringe (glass) with plunger stopper (chlorobutyl rubber) with or without needle in pack sizes of 5 or 10.'

'HDPE bottle with a child-resistant closure and a silica gel desiccant. Pack-sizes of 30, 60 or 90 film-coated tablets.'

All pack sizes should be listed. Pack sizes mentioned should include the number of units, number of doses (for e.g. multi-dose vaccines, inhalers, etc.), total weight or volume of the immediate container, as appropriate, and the number of containers present in any outer carton.

6.6. Special precautions for disposal of a used drug product

Special precautions for disposal of certain products (e.g. cytotoxics or product containing live organism) or waste materials.

Instructions for use/handling
- For preparation before use (e.g. reconstitution or dilution)
- For protection of persons preparing or handling products (including healthcare professionals, parents or carers)
- Information concerning compatibility of product with other drug products or devices

6.7. Drug Product Specification

Reference to relevant current monograph of officially recognized pharmacopeias shall be stated or if the product is non-pharmacopial, drug product specifications table shall be submitted separately as annexure to this section.

7. MARKETING AUTHORISATION / REGISTRATION HOLDER

Name and address of registered Drug Manufacturing Licensee or Importer establishment of the product Registration holder / Marketing Authorisation Holder shall be stated.

8. MANUFACTURER(s)

List the details of manufacturers of Active Pharmaceutical Ingredients / Drug Substance(s) and Finished Drug Product (FDP).

-***For Active Pharmaceutical Ingredients / Drug Substance(s)*** provide the detail like Name of manufacturer, DML number (if applicable), and complete address of manufacturing sites including the manufacturers abroad.

-***For Finished Drug Product (FDP)***, there could be following three situations:-

Self-Manufacturing:
If the applicant is manufacturer itself, then provide the detail including name, DML Number and complete address of the manufacturing site of the applicant (manufacturer).
Contract Manufacturing:
If the applicant is not the manufacturer for the applied product, in such case provide the detail including name DML Number and complete address of the manufacturing site of the manufacturer.
Import:
If the applicant is the importer of the applied product, then provide the details including name of manufacturer and complete address of manufacturing site of manufacturer abroad.

If different operations of manufacturing performed at different sites then detail of all such sites along with details of operation being carried out.

9. REGISTRATION NUMBER / MARKETING AUTHORISATION NUMBER

Registration Number as provided by the DRAP while granting registration / market authorization of the product.

10. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of initial Registration / Marketing Authorisation of the product by DRAP and, if the Registration / Market Authorisation has been renewed, the date of the (last) renewal should be stated in the following example format:

Date of first Registration / Market Authorisation: i.e. **1 June 2014**
Date of latest renewal**:** i.e. **31 May 2019**

11. DATE OF REVISION OF TEXT

Leave blank unless any revision has been incorporated in the SmPC with approval of DRAP. Date of approval of latest revision of SmPC shall be stated.

12. DOSIMETRY (IF APPLICABLE)

Provide details of internal radiation dosimetry in case of radiopharmaceuticals only.

13. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

Additional detailed instructions for extemporaneous preparation and quality control of radiopharmaceutical preparation is required and, where appropriate, maximum storage time during which any intermediate preparation such as an eluate or the ready-to-use pharmaceutical will conform to its specifications.

Special instructions relating to the disposal of containers and unused contents should also be included.

GLOSSARY

ACRONYMS

ADR Adverse Drug Reaction
DRAP Drug Regulatory Authority of Pakistan
DML Drug Manufacturing License
DS Drug Substance
FDP Finished Drug Products
INN International Non-Proprietary Name
MAH Marketing Authorization Holder
PiL Patient information Leaflet
RB Registration Board
RMP Reference Medicinal Product
SmPC Summary of Product Characteristics

DEFINITIONS

Active Pharmaceutical Ingredient (API)

A substance or compound that is intended to be used in the manufacture of a pharmaceutical product as a pharmacologically active compound (ingredient).

Active Moiety:

Active moiety is the part of molecule that is responsible for physiological or pharmacological action of a drug substance.

Container closure system

a) A primary container closure system is a packaging component (for example, a vial) that is in, or may come into, direct contact with the final product dosage form, or components that contribute to the container/closure integrity of the primary packaging material for a sterile product.

b) A secondary container closure system is a packaging component (for example, a carton) that is not, and will not be, in direct contact with the dosage form.

Excipient

Anything other than the Active Pharmaceutical Ingredient(s) / Drug Substance(s) in the dosage form.

Finished Drug Product

A product that has undergone all stages of production, including packaging in its final container and labeling.

Marketing Authorization or Registration

A document issued by the Registration Board set up under the Drugs Act, 1976, as a certificate of drug registration.

Marketing Authorization Holder / Registration Holder

Any person or legal entity that has received marketing authorization/ registration or licensure to manufacture and/or distribute a medicine. It also refers to a person or legal entity allowed to apply for a change to the marketing authorization or registration. Also referred to as the "manufacturer" or "applicant" in this document if both are same.

Medical Dictionary for Regulatory Activities (MedDRA)

MedDRA is a dictionary developed by International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), for validated international medical terminologies used by regulatory authorities and regulatory biopharmaceutical industry through the entire regulatory process.

Officially Recognized Pharmacopoeia (Or Compendium)

The International Pharmacopoeia (Ph. Int.) or such other specifications as published by the World Health Organization, the European Pharmacopoeia (Ph. Eur.), the United States Pharmacopeia (USP), the British Pharmacopoeia (BP), the British Pharmaceutical Codex, the United States National Formulary, the Japanese Pharmacopoeia (JP) and such other publications as may be prescribed.

Packaging Material

Any material, including printed material, employed in the packaging of a pharmaceutical product, excluding, any outer packaging used for transportation or shipment and packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.

Registration Board

A board set up under Section 7 of the Drugs Act, 1976.

Reference Medicinal Product (RMP)

The reference medicinal product is a drug product having same molecules / formulation in the same dosage form which has been granted a market authorization by any of reference drug regulatory agency as adopted by the Registration Board.

Specification

A specification is defined as a list of tests, references to analytical procedures, and appropriate acceptance criteria which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a new drug substance or new drug product should conform to be considered acceptable for its intended use.

OR

Requirements with which the products or materials used or obtained during manufacture must conform as specified in the Drugs (Specifications) Rules 1978.

REFERENCES:

1. The DRAP Act, 2012.
2. The Drugs Act 1976.
3. The Drugs (Licensing, Registering and Advertising) Rules, 1976.
4. The Drugs (Specifications) Rules 1978.
5. European Commission Guidelines on summary of product characteristics, September 2009, Revision 2.
6. WHO Technical Report Series, TRS 993.

Annexure-I

SUMMARY OF PRODUCT CHARACTERISTICS

If the product is subjected to additional monitoring then an inverted equilateral triangular in black font (▼) and the statements shall appear preceding section 1. The black symbol reflects that product is subjected to additional monitoring and allows quick identification of new safety information.

1. **NAME OF DRUG PRODUCT: -**
   (Proprietary / brand) name strength pharmaceutical form
2. **QUALITATIVE AND QUANTITATIVE COMPOSITION: -**
   Name of the Active Pharmaceutical Ingredient(s) / Drug Substance(s)
3. **PHARMACEUTICAL FORM: -**

4. **CLINICAL PARTICULARS: -**
   - **4.1 Therapeutic indications**
   - **4.2 Posology and method of administration**
   - **4.3 Contraindications**
   - **4.4 Special warnings and precautions for use**
   - **4.5 Interaction with other medicinal products and other forms of interaction**
   - **4.6 Fertility, pregnancy and lactation**
   - **4.7 Effects on ability to drive and use machines**
   - **4.8 Undesirable effects**
   - **4.9 Overdose**

5. **PHARMACOLOGICAL PROPERTIES:**
   - **5.1 Pharmacodynamics properties**
     Therapeutic Classification & ATC Codes
   - **5.2 Pharmacokinetic properties**
   - **5.3 Preclinical safety data**

6. **PHARMACEUTICAL PROPERTIES: -**
   - **6.1 List of Excipients**
   - **6.2 Incompatibilities**
   - **6.3 Shelf Life: -**

     The approved shelf-life of this product when packaged and labeled as detailed in the application and modified in subsequent correspondence is as follows: -

Pack (Nature & Content of Container)	**Shelf-life**	**Storage Conditions**
[For example, PVC/Al blisters, 25 and 50 tablets per blister]	18 months	Store below 30^{o}C Protect from moisture
[For example, HDPE bottles]	2 years	Store below 30^{o}C Protect from moisture

6.4 Special precautions for storage

6.5 Nature and contents of container and special equipment for use/administration or Implantation

6.6 Special precautions for disposal

6.7 Drug Product Specification

7. REGISTRATION HOLDER / MARKETING AUTHORIZATION HOLDER:

8. MANUFACTURER: -

Provide the following details of manufacturing sites involved in the manufacturing of Active Pharmaceutical Ingredients / Drug Substance(s) and finished drug product. In case multiple manufacturers are involved, provide details for each. The name, address and responsibility of each manufacturer including contractors and each proposed production site or facility involved in manufacturing and testing should be provide.

Name of Ingredient / Constituent of Drug Product	**Name of Manufacturing Site**	**Address of site**	**Manufacturing step (if applicable)**
[Active Pharmaceutical Ingredients / Drug Substance(s) I]			Production
[Active Pharmaceutical Ingredients / Drug Substance(s) II]…..			Production
Half-finished drugs e.g. Pellets			[For example, granulation]
Finished product			

9. REGISTRATION / MARKETING AUTHORIZATION NUMBER: -

10. DATE FROM WHICH MARKETING IS AUTHORIZED:

11. DATE OF REVISION OF THE TEXT: -