



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Section 6: Pharmaceutical particulars

Rev. 1

SmPC training presentation

Note: for full information refer to the European Commission's [Guideline on summary of product characteristics \(SmPC\)](#)

SmPC Advisory Group

An agency of the European Union





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6.1 List of excipients

- **All excipients**
 - Even those present in small amounts
 - Including ingredients of printing inks, or, other excipient mixtures (e.g. ingredients of flavour), except if not known or too complex (unless contains excipient of known effect)
- Use INN + salt or hydrate or European Pharmacopoeia name or common name
- Where relevant:
 - Indicate '(for pH-adjustment)'
 - Add E numbers (e.g. excipient of known effect)
 - Declare chemically modified excipients (e.g. 'pregelatinised starch')

SmPC
examples
[1 excipients](#)
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In case of a product containing a covert marker for the purpose of tracking, tracing and authentication, a general term such as Authentication factor should be included instead of the name of the excipient, unless the excipient is one that is known to have a recognised action or effect

Not to be listed (e.g. residues of substances used during manufacture): see details in guideline



Example 1-list of excipients

Active substance X 0.5 mg prolonged-release hard capsules

6.1 List of excipients

Capsule content:

Hypromellose
Ethylcellulose
Lactose monohydrate
Magnesium stearate.

Capsule shell:

Titanium dioxide (E 171)
Yellow iron oxide (E 172)
Red iron oxide (E 172)
Sodium laurilsulfate
Gelatin.

Printing ink(Opacode S-1-15083):

Shellac
Lecithin (soya)
Simeticone
Red iron oxide (E 172)
Hydroxypropylcellulose.



Example 2-list of excipients

Active substance X 1000 IU/0.5 ml solution for injection in a pre-filled syringe

6.1 List of excipients

Sodium dihydrogen phosphate dihydrate

Disodium phosphate dihydrate

Sodium chloride

Glycine

Polysorbate 80

Water for injections

Hydrochloric acid (for pH-adjustment)

Sodium hydroxide (for pH-adjustment)



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, particularly those which are 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
- When appropriate, the following **standard statements** may be added:
 - *'In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products'*
 - *'This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6'*

SmPC examples
[3 incompatibilities](#)



Example 3-incompatibilities

Active substance X 30 MIU/0.5 ml solution for injection or infusion

6.2 Incompatibilities

Active substance X should not be diluted with sodium chloride solution. This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Diluted active substance X may be adsorbed to glass and plastic materials except diluted, as mentioned in section 6.6.



6.3 Shelf life

- Shelf life for medicinal product **as packaged for sale**
- If appropriate
 - Shelf-life **after dilution or reconstitution or after first opening**. See [Note for guidance on maximum shelf life for sterile products for human use after first opening or following reconstitution](#)
 - If **different concentration need to be prepared**, e.g. for use in children, the physiochemical stability throughout entire concentration range for different concentrations should be stated
e.g. *"The stability has been demonstrated between x mg/ml and y mg/ml for t hours/days at 25 °C and 2-8 °C"*
 - In case **specific temporary storage conditions** need to be provided to healthcare professionals or patients, e.g. *"for the purpose of ambulatory use (e.g. shelf-life 24 months at 2-8°C of which 3 months could be below 25°C)"*, specific additional guidance should be provided as appropriate
 - **In-use shelf life of a device** supplied with a medicinal product

SmPC examples

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Example 4–shelf life

Active substance X 0.5 mg prolonged-release hard capsules

6.3 Shelf life

3 years

After opening the aluminium wrapper: 1 year



Example 5–shelf life

Active substance X 5 mg/ml powder for suspension for infusion

6.3 Shelf life

Unopened vials: 2 years

Stability of reconstituted suspension in the vial:

After first reconstitution, the suspension should be filled into an infusion bag immediately. However, chemical and physical in use stability has been demonstrated for 8 hours at 2°C–8°C in the original carton, and protected from bright light. Alternative light-protection may be used in the clean room.

Stability of the reconstituted suspension in the infusion bag:

After reconstitution, the reconstituted suspension in the infusion bag should be used immediately. However chemical and physical in use stability has been demonstrated for 8 hours not above 25°C.



6.4 Special precautions for storage

Storage warnings should use one or more of the **standard statements**

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Explanation specifying whether the product is sensitive to light and/or moisture should be added.

See [Note for guidance on declaration of storage conditions in the product information of medicinal products](#)

See [Appendix III, QRD product information template](#)

SmPC examples

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



Example 6—special precautions for storage

Active substance X 200 mg dispersible tablets

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C)

After first opening of the tablet container:

Do not refrigerate.

Do not store above 30°C.

Keep the container tightly closed in order to protect from moisture.



Example 7—special precautions for storage

Active substance X 5 micrograms/0.5 ml suspension for injection

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.



Example 8—special precautions for storage

Active substance X 10 mg tablets

6.4 Special precautions for storage

Do not store above 30°C.

Store in the original package in order to protect from moisture.

Keep the bottle tightly closed.



Example 9—special precautions for storage

Active substance X 9 microgram/strain suspension for injection Influenza vaccine

6.4 Special precautions for storage

Store in a refrigerator (2°C-8°C). Do not freeze.

Keep the syringe in the outer carton in order to protect from light.



Example 10—special precautions for storage

Active substance X 150 mg powder for solution for injection

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Store in the original package in order to protect from light.

For storage conditions of the reconstituted medicinal product, see section 6.3.



6.5 Nature and contents of container

- **Immediate container:**
 - See European Pharmacopoeia standard term
 - State material of construction (e.g. glass vials, PVC/Aluminium blisters, HDPE bottles)
 - State enclosure colour for parenteral preparations, when used to differentiate between presentations of a product. Indicate if closure is child-resistant if appropriate
- Any **other component** of product e.g.
 - Description of container of solvent
 - Needles, swabs, measuring spoons, syringes, inhaler devices, desiccant
- List **all pack sizes**
 - For each pack size: number of units, number of doses, total weight or volume of immediate container and number of containers present in any outer carton if appropriate
- Include a **standard statement** 'Not all pack sizes may be marketed' if appropriate

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Example 11–nature and contents of container

SmPC guideline

Example text for 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.'



Example 12–nature and contents of container

Active substance X 1 g oral powder

6.5 Nature and contents of container

HDPE bottles with a child resistant closure.

Each pack contains 1 bottle with 180 g of powder.

Three measuring spoons are included in each pack.



Example 13–nature and contents of container

Active substance X 0.5 mg prolonged-release hard capsules

6.5 Nature and contents of container

Transparent PVC/PVDC aluminium blister wrapped in an aluminium pouch with a desiccant containing 10 capsules per blister.

Pack sizes: 30, 50, 60 and 100 prolonged-release hard capsules.

Not all pack sizes may be marketed



Example 14–nature and contents of container

Active substance X 5 mg/ml powder for suspension for infusion

6.5 Nature and contents of container

50 ml vial (type 1 glass) with a stopper (butyl rubber), with an overseal (aluminium), containing 100 mg active substance X.

Pack size of one vial.



Example 15–nature and contents of container

Active substance X 0.25 mg powder and solvent for solution for injection

6.5 Nature and contents of container

Packs with 1 or 7 Type I glass vials sealed with a rubber stopper.

Additionally for each vial the packs contain:

1 pre-filled syringe (Type I glass cartridge closed with rubber stoppers) with 1 ml solvent for parenteral use

1 injection needle (20 gauge)

1 hypodermic injection needle (27 gauge)

2 alcohol swabs.

Not all pack sizes may be marketed.



6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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

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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 medical products or devices

Appearance of product after reconstitution should be stated

In exceptional cases, where a product is indicated in children and no adequate paediatric formulation can be developed, information on **extemporaneous formulation** should appear under a sub-heading **“Use in the paediatric population”** and cross-refer to 4.2

If there are no special use or handling instructions for the pharmacist or other healthcare professionals, the **standard statement**, ‘No special requirements.’ should be included



Example 16—special precautions

Active substance X 1 mg/5 ml powder and solvent for solution for infusion

6.6 Special precautions for disposal and other handling

When preparing and handling active substance X solutions, the use of gloves is recommended. If active substance X dry powder or reconstituted solution should come into contact with the skin or mucous membranes, they should be washed thoroughly with water.

Instructions for reconstitution

Active substance X should be reconstituted by adding 5 ml of the provided solvent for parenteral use (sodium chloride 9 mg/ml (0.9%) solution for injection). A homogeneous solution will be obtained by shaking gently. The solution of the reconstituted product should be inspected visually for particulate matter prior to administration. The solution has a clear to light yellow colour. The formulation does not contain a preservative and is for single use only. Once opened, the content of a vial should normally be used immediately (see section 6.3). For instructions on administration, see section 4.2.

Disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

Section 4.2

Method of administration

For instructions on reconstitution prior to administration, see section 6.6.



Example 17—special precautions

Active substance X 500 mg tablets

Section 6.6 Special precautions for disposal and other handling

This medicinal product should not be handled by persons other than the patient and his/her caregivers, and especially not by pregnant women. Caregivers should wear disposable gloves when handling the tablets.

Section 4.2

Method of administration

The total daily dose may be divided in two or three doses according to patient's convenience. Tablets should be taken with water during meals containing fat-rich food (see section 4.5). Patients should be advised not to use any tablets showing signs of deterioration, and caregivers to wear disposable gloves when handling the tablets.



Example 18–special precautions

Active substance X

6.6 Special precautions for disposal

Apply immediately upon removal from the protective sachet. After use the patch still contains substantial quantities of active ingredients. Remaining hormonal active ingredients of the patch may have harmful effects if reaching the aquatic environment. Therefore, the used patch should be discarded carefully. The disposal label from the outside of the sachet should be peeled open. The used patch should be placed within the open disposal label so that the sticky surface covers the shaded area on the sachet. The disposal label should then be closed sealing the used patch within. Any used or unused patches should be discarded according to local requirements or returned to the pharmacy. Used patches should not be flushed down the toilet nor placed in liquid waste disposal systems.



FAQs

1. How should lactose monohydrate be expressed in the SmPC?
2. Should gases present in a medicinal product mainly as propellant be listed in section 6.1?*
3. How should information on capsule shells and their components be stated in the SmPC for dry powder inhalers?*
4. Is it acceptable to include latex-free statements in section 6.5?
5. Which material of construction should be described in section 6.5 of the SmPC?
6. Should information on the measuring devices be provided in the SmPC?
7. Should instructions for use administration be presented in section 4.2 or 6.6?*
8. Should information about the needle safety system be communicated in the SmPC?*



1. How should lactose monohydrate be expressed in the SmPC?

- **Sections 2 and 6.1** of the SmPC pertain to the exact composition of the medicinal product, where the excipients have to be expressed qualitatively, i.e. lactose monohydrate. As lactose also needs to be expressed quantitatively in section 2 as it is an excipient with known effect, it should be presented as “x mg lactose (as monohydrate)” considering that the relevant amount for clinical practice is the amount of lactose. In **section 4.4**, information on excipients is given to warn on their known effects, therefore, in this section, the excipient should be expressed as referred to in the [“Guideline on the excipients in the label and package leaflet of the medicinal product for human use”](#); i.e. lactose



2. Should gases present in a medicinal product mainly as propellant be listed in section 6.1?*

- The SmPC guideline requires that all the excipients, which are present in the product, should be listed qualitatively in section 6.1, even those present in small amounts.
- Although propellants differ from the usual absorbed excipients, they may still come into contact with the patient even if its for a short time and in a limited amount. Furthermore, propellants may also be flammable which may require special precautions for handling or storage, to be communicated with appropriate warnings. Propellants should therefore be listed qualitatively in section 6.1 and specified as such (e.g. in adding "*propellant*") after the name of the gas).



3. How should information on capsule shells and their components be stated in the SmPC for dry powder inhalers? *

- For inhalation powders in hard capsules the capsule shell is considered as an excipient and the components should be stated in section 6.1. of the SmPC under a separate subheading "Capsule shell".



4. Is it acceptable to include latex-free statements in section 6.5?

- Section 6.5 should provide information on the material of construction of the immediate container and any other component of the product should be listed. Therefore, if the immediate container contains latex, this information should be highlighted with the related warning as per the guideline on “Excipients in the label and package leaflet of medicinal products for human use”
- There is **no ground or need to include additional information regarding the absence of a component in a container** e.g. absence of latex, as the SmPC is the source of what the medicinal product is and contains and how it should be used. Furthermore, it is not relevant to include information on what is not included in a medicinal product as the information may become extensive and confusing



5. Which material of construction should be described in section 6.5 of the SmPC?

- The SmPC guideline recommends that reference should be made to the immediate container; **the material of construction of the immediate container** should be stated **and any other component of the product** should be listed e.g. needles, syringes, measuring devices as they will come into contact with the medicinal product and for a short time, they will become the immediate container of the product.



6. Should information on the measuring devices be provided in the SmPC?

- The SmPC guideline recommends in section 6.5 “Nature and contents of the container” to explain the **graduation on the measuring devices** which should be consistent with the posology recommendations



7. Should instructions for use administration be presented in section 4.2 or 6.6?*

- As general guidance, information on administration is to be included in section 4.2, whereas information on preparation 6.6.
- Precautions related to the administration of the product, e.g. precaution to be taken to improve tolerance (e.g. slow infusion), interference with other products (e.g. need to separate times of administration of eye drops) or advice on safe handling (e.g. to prevent contamination) should be mentioned in section 4.2, under the subheading “Method of administration”, in explaining the reason of the precaution of the product, a cross reference to section 6.6 should be included. The precautions can be repeated or further detailed when describing instructions for use in 6.6 to prevent healthcare professionals from missing information.
- The advice for safe handling and administration of the medicinal product also be clearly communicated in the package leaflet.



8. Should information about the needle safety system be communicated in the SmPC? *

- Yes, the information about the needle safety system should be communicated in the SmPC. Please see more information in the following links:
 - Quality medicines questions and answers: Part 2, [Specific types of product - Needle safety systems](#) and [Compilation of QRD decisions on stylistic matters in product information](#) for medical products with presentations containing syringes with or without needle guard.



Thank you for consulting this training presentation

SmPC Advisory Group

Please note the presentation includes examples that may have been modified to best illustrate the related principle