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SCIENCE MEDICINES HEALTH

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Human Medicines Division

Questions and answers on labelling requirements for centrally authorised metered dose inhalers containing fluorinated greenhouse gases

Quality Review of Documents (QRD) group

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1. Introduction

The European Medicines Agency (EMA) together with the Member States, in the context of the Quality Review of Documents (QRD) group, have developed this Questions and Answers (Q&A) document with the aim to provide operational guidance on labelling requirements for metered dose inhalers containing fluorinated greenhouse gases (F-gases). The topics addressed in the present document are primarily based on the European Commission's policy on fluorinated greenhouse gases and its legal framework, the F-gas Regulation (EU) 2024/573 and its implementation acts.

Any applicant/marketing authorisation holder (MAH) who has difficulties applying the below guidance, may contact EMA (QRD@ema.europa.eu).

2. Questions and answers on labelling requirements

2.1. How does the implementation of the F-gas Regulation (EU) 2024/573 impact metered dose inhalers?

As of 1 January 2025, any metered dose inhalers containing fluorinated greenhouse gases, such as hydrofluorocarbons (HFC), must comply with Regulation (EU) 2024/573. In this context, all metered dose inhalers containing these gases shall be labelled according to the requirements as set out in that Regulation and the Commission Implementing Regulation (EU) 2024/2174 determining the format of the labels.

2.2. How should metered dose inhalers containing fluorinated greenhouse gases be labelled?

Article 12 of Regulation (EU) 2024/573 contains a set of legal requirements that is newly applicable to the labelling and package leaflet of metered dose inhalers containing fluorinated greenhouse gases. These legal requirements are translated into standard statements to be included in the product information, specifically Annexes IIIA (labelling) and IIIB (package leaflet). The standard statements must be printed in the language(s) already used on the packaging.

2.2.1. Annex IIIA (labelling):

In accordance with Article 12(3) of Regulation (EU) 2024/573 and the Commission Implementing Regulation (EU) 2024/2174 determining the format of the labels, the following standard statements should be included in section 3 (list of excipients) of the outer carton, or section 6 (other) of the immediate packaging, if space permits:

- "contains fluorinated greenhouse gases."
- "Each inhaler contains {X} <g><kg> of {fluorinated greenhouse gas name} corresponding to {Y} tonne CO_2 equivalent (global warming potential GWP = {Z})."

The accepted industry designation for the fluorinated greenhouse gases concerned (e.g. HFC-134a), or, if no such designation is available, the chemical name must be mentioned too.

In case of space constraints, the statement "contains fluorinated greenhouse gases" may appear only on the outer carton provided that the package leaflet contains all the statements above (see section 2.2.2).

The font size should not be smaller than the minimum size of other information on the immediate packaging or outer carton (depending on where the information required by the F-gas legislation is placed).

2.2.2. Annex IIIB (package leaflet):

In accordance with Article 12(16) of Regulation (EU) 2024/573 and the Commission Implementing Regulation (EU) 2024/2174 determining the format of the labels, the following standard statements should be included in section 6 (contents of the pack and other information) of the package leaflet under the subheading "What {product name} contains":

- "This medicine contains fluorinated greenhouse gases."
- "Each inhaler contains {X} <g><kg> of {fluorinated greenhouse gas name} corresponding to {Y} tonne CO_2 equivalent (global warming potential GWP = {Z})."

The accepted industry designation for the fluorinated greenhouse gases concerned (e.g. HFC-134a), or, if no such designation is available, the chemical name must be mentioned too.

The font size should not be smaller than the minimum size of other information on the package leaflet.

Translations of the above standard statements into all EU/EEA official languages are available in the "QRD statements for metered dose inhalers containing fluorinated greenhouse gases" (EMA/355151/2024).

2.3. Which regulatory procedure should be used to have the product information of metered dose inhalers containing fluorinated greenhouse gases comply with the new labelling requirements?

2.3.1. Pre-authorisation phase

Any new or ongoing marketing authorisation applications for metered dose inhalers containing fluorinated greenhouse gases for which the CHMP Opinion is expected after 1 January 2025 should comply with the new legal requirements and include the relevant standard statements in their product information (PI), i.e. Labelling (Annex IIIA) and Package leaflet (Annex IIIB).

Applicants are also reminded that they have the obligation to provide translations of the Product Information annexes into all EU/EEA official languages, as per standard post-opinion procedure.

2.3.2. Post-authorisation phase

For authorised metered dose inhalers containing fluorinated greenhouse gases with ongoing variations affecting annexes, the corresponding wording should be introduced as part of the ongoing procedure. The scope of the applied variation should include the information on compliance with the Regulation (EU) 2024/573.

For any other authorised metered dose inhalers with no ongoing variation, a notification under article 61(3) of the Directive 2001/83/EC should be submitted.

2.4. By which date should these new labelling requirements be implemented?

According to Article 38 of Regulation (EU) 2024/573, the new labelling requirements laid down in the Article 12 should apply from 1 January 2025. MAHs of metered dose inhalers containing fluorinated greenhouse gases must initiate the relevant processes to comply with the new requirements as soon as possible. This includes the regulatory procedures described under section 2.3.

MAHs should ensure that documented evidence of change management is kept and provided to competent authorities at their request.

2.5. Which data should be submitted to replace the fluorinated greenhouse gases in metered dose inhalers?

For replacing the fluorinated greenhouse gases in metered dose inhalers (e.g. when transitioning to low global warming potential propellant), a separate Q&A document was developed to provide advice regarding data requirements for such replacements.

The Questions and answers on data requirements when transitioning to low global warming potential (LGWP) propellants in oral pressurised metered dose inhalers were prepared in anticipation of the implementation of Regulation (EU) 2024/573.