DECISION

No. 8/26.06.2009

on the approval of the Guideline on the readability of the labelling and package leaflet of medicinal products for human use

The Scientific Council of the National Medicines Agency, set up based on Minister of Public Health Order no. 1027/22.05.2008, as amended, reunited on summons of the National Medicines Agency President in the ordinary meeting of 26.06.2009, in accordance with Article 10 of Government Ordinance no. 125/1998 related to the set up, organisation and functioning of the National Medicines Agency, approved as amended through Law No. 594/2002, as further amended, agrees on the following

DECISION

Single Article – The Guideline on the readability of the labelling and package leaflet of medicinal products for human use is approved, according to the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Medicines Agency

Acad. Prof. Dr. Victor Voicu

ANNEX

Guideline on the readability of the labelling and package leaflet of medicinal products for human use

CHAPTER I
Introduction and legal basis

Art. 1. – This Guideline is a translation into Romanian and an adaptation of those parts in the „Guideline on the readability of the labelling and package leaflet of medicinal products for human use" EC/2009, which have not yet been adapted as a NMA Scientific Council Decision.

Art. 2. – According to Art. 763, 764 and 769 of Law No. 95/2006 on healthcare reform, Title XVII – The medicinal product, as further amended, (hereinafter Law No. 95/2006), transposing Art. 54, 55 and 59 of Directive 2001/83/EC, all medicinal products authorised for marketing should be accompanied by a secondary/primary packaging and by the leaflet.

Art. 3. - Art. 768 of Law No. 95/2006 transposing Art. 58 of Directive 2001/83/EC, allows for the omission of a package leaflet where all the required information can be directly conveyed on the packaging.

Art. 4. – According to Art. 765 of Law No. 95/2006, transposing Art. 56 of Directive 2001/83/EC, the particulars to be included in the labelling shall be easily legible, clearly comprehensible and indelible.

Art. 5. - Art. 771 (1) and 702 (4)(m) of Law No. 95/2006, transposing Art. 61 (1) and 8(3) of Directive 2001/83/EC, mentions that, at the same time with the submission of the marketing authorisation application, one or several mock-ups of the medicinal product's outer and inner packaging, accompanied by the project of the leaflet, should be submitted to the National Medicines Agency (NMA).

Art. 6. - Art. 773 (1) of Law No. 95/2006, transposing Art. 63 (1) of Directive 2001/83/EC requires that the labelling information shall appear in Romanian; additional languages can be included provided the information presented is the same in all languages.

Art. 7. - Art. 773 (2) of law No. 95/2006, transposing Art. 63 (2) of Directive 2001/83/EC, stipulates the fact that the leaflet should be edited and conceived in order to be clear and easily understood, allowing the users to take appropriate action, when needed, with the help of healthcare professionals; the leaflet should be clear and easily readable in Romanian.

CHAPTER II
Scope

Art. 8. - The main purpose of this Guideline is to provide guidance on how to ensure that the information on the labelling and package leaflet is accessible to and can be understood by those who receive it, so that they can use their medicinal product safely and appropriately.

Art. 9. - This guideline is written to assist applicants and marketing authorisations holders when drawing up the labelling and package leaflet and preparing the mock-ups or specimens of the sales presentations.

Art. 10. - The guidance gives advice on the presentation of the content of the labelling and package leaflet (required in accordance with Chapter V of Law No. 95/2006, Title XVII – The medicinal product, transposing Title V of the Directive) and on the design and layout concepts which will aid the production of quality information.

Art. 11. - This Guideline is published in accordance with Article 775(c) of Law No. 95/2006, transposing Art. 65 (c) of Directive 2001/83/EC, which provides for the development of guidelines concerning the legibility of particulars on the labelling and package leaflet.

Art. 12. - The Guideline is intended to apply to all marketing authorisation procedures and to all medicinal products, including those available without medical prescription.

CHAPTER III
Recommendations for the package leaflet

III.1. General considerations

Art. 13. - (1) The package leaflet is intended for the patient/user.

(2) A well designed and clearly worded package leaflet maximises the number of people who can use the information, including older children and adolescents, those with poor literacy skills and those with some degree of sight loss.

(3) Companies are encouraged to seek advice from specialists in information design when devising their house style for the package leaflet to ensure that the design facilitates navigation and access to information.

Art. 14. – The following Guideline sets out recommendations on various aspects related to the preparation of package leaflets; it is aimed at helping applicants/marketing authorization holders to fully comply with the legal requirements and is based on experience where it has been shown that using these techniques optimises the usability of the package leaflet.

Art. 15. - Additional requirements may apply in Romania; applicants should check details of those requirements in the Notice to Applicants (NtA), Volume 2A, chapter 7.

III.2. Type size and font

Art. 16. – (1) Choose a font which is easy to read.

(2) Stylised fonts which are difficult to read should not be used.

(3) It is important to choose a font in which similar letters/numbers, such as "i", "l" and "1" can be easily distinguished from each other.

Art. 17. – (1) The type size should be as large as possible to aid readers.

(2) A type size of 9 points, as measured in font 'Times New Roman', not narrowed, with a space between lines of at least 3 mm, should be considered as a minimum.

(3) However, for marketing authorization applications until 1 February 2011, a type size of 8 points, as measured in font 'Times New Roman', not narrowed, with a space between lines of at least 3 mm, should be acceptable as absolute minimum.

Art. 18. - Consideration should be given to using different text sizes to enable key information to stand out and to facilitate navigation in the text (for example, for headings).

Art. 19. - Consideration should be given to using larger type size where a medicinal product is especially intended for an indication linked to visual impairment [see "Guidance concerning the Braille requirements for labelling and the package leaflet", Art. 14 (1)].

Art. 20. – (1) The widespread use of capitals should not occur.

(2) The brain recognises words in written documents by the word shape, so choose lower case text for large blocks of text; however, capitals may be useful for emphasis of the text.

Art. 21. - (1) Do not use italics and underlining as they make it more difficult for the reader to recognize the word-shape.

(2) Italics, however, may be considered when using Latin terms.

III.3. Design and layout of the information

Art. 22. - The use of "justified" text, that is text aligned to both left hand and right hand margins, should in principle not be used.

Art. 23. – (1) Line spaces should be kept clear; the space between lines is an important factor influencing the clarity of the text.

(2) As a general rule the space between one line and the next should be at least 1.5 times the space between words on a line, where practical.

Art. 24. – (1) Contrast between the text and the background is important.

(2) Factors like paper weight, colour of the paper, size and dimension of the type and the paper itself should be considered.

(3) Too little contrast between the text and the background adversely affects the accessibility of the information.

(4) Therefore, background images should in principle not be placed behind the text since they may interfere with the clarity of the information making it harder to read.

Art. 25. – (1) A column format for the text can help the reader navigate the information easier.

(2) The margin between the columns should be large enough to adequately separate the text.

(3) If space is limited a vertical line to separate the text may be used.

(4) Related information should be kept together so the text flows easily from one column to the next.

(5) Consideration should be given to using a landscape layout which can be helpful to patients.

(6) Where a multilingual leaflet is proposed there should be a clear demarcation between the different languages used; all the information provided in each language should be assembled.

III.4. Headings

Art. 26. – (1) Headings are important and can help patients navigate the text if used well; therefore, bold type face for the heading or a different colour may help make this information stand out.

(2) The spacing above and below the headings should be consistently applied throughout the leaflet.

(3) Same level headings should appear consistently (numbering, bulleting, colour, indentation, font and size) in order to aid the reader.

Art. 27. – (1) The use of multiple levels of headings should be considered carefully, as more than two levels may make it difficult for readers to find their way around the leaflet.

(2) However, where complex information has to be communicated multiple levels of headings may be needed.

(3) Using lines to separate the different sections within the text can also be helpful as a navigational tool.

Art. 28. – (1) Include all main section headings covered by Art. 769 (1) of Law No. 95/2006, transposing Art. 59(1) of Directive 2001/83/EC within the leaflet.

(2) Sub-headings and associated text within the leaflet should only be included if these are relevant for the particular medicinal product; for example if there is no information in related to excipients of known effect this section may be omitted from the package leaflet.

III.5. Print colour

Art. 29. – (1) Accessibility is not only determined by print size.

(2) Characters may be printed in one or several colours allowing them to be clearly distinguished from the background.

(3) A different type size or colour is one way of making headings or other important information clearly recognisable.

Art. 30. – (1) The relationship between the colours used is as important as the colours themselves.

(2) As a general rule dark text should be printed on a light background.

(3) However, there may be occasions when reverse type (light text on a dark background) could be considered to highlight for instance particular warnings; in such circumstances the quality of the print will need careful consideration and may require the use of a larger type size or bold text.

Art. 31. - Similar colours should not be used for the text and background as legibility is impaired.

III.6. Syntax

Art. 32. – Some people may have poor reading skills, and some may have poor health literacy; therefore, aim to use simple words of few syllables.

Art. 33. – (1) Long sentences should not be used.

(2) It is better to use a couple of sentences rather than one longer sentence, especially for new information.

Art. 34. – (1) Long paragraphs can confuse readers, particularly where lists of side effects are included.

(2) The use of bullet points for such lists is considered more appropriate; where possible, no more than five or six bullet points in a list are recommended.

Art. 35. – (1) When setting out the side effects it is particularly important to consider the order in which they are given so the patients/users may maximise the use of the information.

(2) In general, setting out the side effects by frequency of occurrence, starting with the highest frequency, is recommended to help communicate the level of risk to individuals.

(3) Frequency terms should be explained in a way patients/users can understand – for example “very common” (more than 1 in 10 patients).

(4) However, where serious side effects exist which would require the patient/user to take urgent action this should be afforded greater prominence and appear at the start of the section.

(5) Setting side effects by organ/system/class is not recommended since patients/users are in general not familiar with these classifications.

III.7. Style

Art. 36. - When writing, an active style should be used, instead of passive. For example:

- *"Take 2 tablets"* instead of *"2 tablets should be taken"*,
- *"You must…'* instead of *'it is necessary…."*

Art. 37. – (1) When telling patients what action to take, reasons should be provided.

(2) Instructions should come first, followed by the reasoning, for example: 'take care with X if you have asthma – it may bring on an attack'.

Art. 38. - "Your medicinal product, this medicinal product, etc." should be used rather than repeating the name of the medicinal product, as long as the context makes clear what is being referred to.

Art. 39. – (1) Abbreviations and acronyms should not usually be used unless these are appropriate.

(2) When first used in the text, the meaning should be spelled out in full.

(3) Similarly scientific symbols (e.g. > or <) are not well understood and should not be used.

Art. 40. – (1) Medical terms should be translated into language which patients can understand.

(2) Consistency should be assured in how translations are explained by giving the lay term accompanied by a description first and the detailed medical term immediately after.

(3) On a case by case basis the most appropriate term (lay or medical) may then be used thereafter throughout the package leaflet in order to achieve a readable text.

(4) Make sure that the language used alerts the reader to all the information relevant to him/her, and provides sufficient detail on how to recognise possible side effects and understand any action which may be necessary.

III.8. Paper

Art. 41. – (1) The chosen paper weight should be such that the paper is sufficiently thick to reduce transparency which makes reading difficult, particularly where the text size is small.

(2) Glossy paper reflects light, making the information difficult to read, so the use of uncoated paper should be considered.

Art. 42. - Make sure that when the leaflet is folded the creases do not interfere with the readability of the information.

III.9. Use of symbols and pictograms

Art. 43. – (1) The legal provisions within Art. 772 of Law No. 95/2006, transposing Art. 62 of Directive 2001/83/EC permit the use of images, pictograms and other graphics to aid comprehension of the information, but these exclude any element of a promotional nature.

(2) Symbols and pictograms can be useful provided the meaning of the symbol is clear and the size of the graphics/drawings makes it easily legible.

(3) These should only be used to aid navigation of the text, as well as to clarify or highlight certain aspects of the text and should not replace the actual text.

(4) Evidence may be required to ensure that their meaning is generally understood and not misleading or confusing; if there is any doubt about the meaning of a particular pictogram it will be considered inappropriate.

(5) Particular care will be needed when symbols are transferred or used in other language versions of the leaflet and additional user testing of these may be necessary.

III.10. Additional information

III.10.1. Medicinal product ranges

Art. 44. – (1) There should, in principle, be a separate leaflet for each strength and pharmaceutical form of a medicinal product.

(2) On a case-by-case basis national competent authorities or the European Commission may however agree to allow the use of combined package leaflets for different strengths and/or different pharmaceutical forms (e.g. tablets and capsules), for instance where achieving a recommended dose necessitates a combination of different strengths, or when the dose varies from day to day depending on the clinical response.

Art. 45. - Simple reference to other strengths and pharmaceutical forms of the same medicinal product is always possible if necessary for the therapy; for instance, referring to a different strength, or referring in the package leaflet of a tablet which is unsuitable for children to the availability of an oral solution for children.

III.10.2. Medicinal products administered by a healthcare professional or in a hospital

Art. 46. – (1) For medicinal products administered by a healthcare professional, information from the summary of product characteristics for the healthcare professional (e.g. the instructions for use) could be included at the end of the patient leaflet e.g. in a tear-off portion, to be removed prior to giving the leaflet to the patient.

(2) Alternatively the complete summary of product characteristics could be provided in the pack along with the package leaflet.

Art. 47. - For medicinal products administered in hospital, additional package leaflets (in addition to the one provided in the pack) may be made available on request to ensure that every patient receiving the medicinal product has access to the information.

III.11. Templates for the package leaflet

Art. 48. - The template provided in Romanian on the NMA Website (http://www.anm.ro) reflects the particulars which must appear on the labelling and package leaflet of medicinal products according to Law No. 95/2006, transposing Directive 2001/83/EC; these will help to ensure that the information appears as intended by the Directive.

Art. 49. - For the purpose of regulatory submissions to national competent authorities/EMEA, the text version of the medicinal product information is to be presented in a certain format and lay-out (see "QRD convention" on the EMEA Website at http://www.emea.europa.eu/htms/human/qrd/qrdplt/qrdconvention.pdf) using the electronic product information templates.

Art. 50. – (1) When using these templates, reference should be made to relevant Community Guidelines, QRD Guidelines and the "Annotated QRD Template", which provides detailed guidance on how to complete each section and which can be found on the EMEA Website (http://www.emea.europa.eu/htms/human/qrd/qrdplt/AnnotatedTemplate-H.pdf) and the Heads of Agencies Website (http://www.hma.eu/uploads/media/QRD_annotated_template_CMDh.pdf).

Art. 51. – (1) Having used the templates provided, marketing authorisation applicants/holders will still need to format the resulting text into the relevant full colour mock-ups or specimens of the package leaflet.

(2) Also applicants should remember that using the templates does not guarantee compliance with Article 769 (3) of Law No. 95/2006, transposing Art. 59 (3) of the directive and consultations with target patient groups will

still have to be carried out on the full colour mock-up or specimen of the package leaflet.

CHAPTER IV
Recommendations for the labelling

IV.1. General considerations

Art. 52. – (1) Labelling covers both outer packaging and inner packaging.

(2) Although inner packaging may include a lesser set of particulars, many of the principles outlined in relation to outer packaging will apply equally to the labelling of blister packs or other small package units.

Art. 53. - Labelling ensures that the critical information necessary for the safe use of the medicinal product is legible, easily accessible and that users of the medicinal product are assisted in assimilating this information so that confusion and error are minimised.

Art. 54. - Those involved in the design of labelling should consider the following sections prior to Submission of the documents to the competent authority.

a) The recommendations given in relation to the package leaflet (chapter III) may also be applicable to labelling and should be borne in mind in designing and laying out the required information on labels.

b) The particulars appearing on the label of all medicinal products should be printed in characters of at least 7 points (or of a size where the lower case "x" is at least 1.4 mm in height), leaving a space between lines of at least 3 mm.

Art. 55. - In particular the information presented on small packs will need careful consideration so that the text is presented in as large a type size as possible to reduce the likelihood of medication error.

Art. 56. – (1) According to Article 767 of Law No. 95/2006, transposing Art. 57 of Directive 2001/83/EC, additional labelling requirements may apply in Romania in respect of legal status for supply and identification and authenticity of medicinal products.

(2) Applicants should check details of those requirements in Chapter VI of Title XVII – The medicinal product of Law No. 95/2006.

Art. 57. – (1) Labelling must contain all elements required by Article 763 of Law No. 95/2006, transposing Art. 54 of Directive 2001/83/EC or a lesser set of elements where the provisions of Article 764 of Law No. 95/2006, transposing Art. 55 of the same Directive apply.

(2) Nevertheless, of the information items listed in Article 763 of Law No. 95/2006, transposing Art. 54 of Directive 2001/83/EC, certain items are deemed critical for the safe use of the medicinal products; these items are:

- Name of the medicinal product;
- Strength and, where relevant, total content
- Route of administration.

Art. 58. - Where possible, these elements should be brought together using a sufficiently large type size on the labelling. Having these items together in the same field of view suffices in order to aid users.

IV. 2. Commercial name of the medicinal product

Art. 59. – (1) Article 763 (a) of Law No. 95/2006, transposing Art. 54 (a) of Directive 2001/83/EC sets out the requirements in relation to the commercial name of the medicinal product.

(2) In accordance with these provisions, the full name of the medicinal product, with its strength and its pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults, should appear on the outer packaging and on the immediate packaging to aid accurate identification of the medicinal product.

Art. 60. – (1) Where the medicinal product contains up to three active ingredients, the INN/common name(s) of these active ingredient(s) should be stated after the full name on the outer packaging and the immediate packaging, unless the INN/common name(s) is part of the commercial name.

(2) The INN should be appropriately emphasised for safety reasons.

Art. 61. - For requirements concerning Braille, see SCD No. 12/15.06.2007 on the approval of the Guideline on the enforcement of legal provisions concerning the Braille requirements for labelling and the package leaflet of medicinal products, based on the European Commission Guideline called "Guidance concerning the Braille requirements for labelling and the package leaflet" (Article 56a of Directive 2001/83/EC).

IV. 3. Strength and total content

Art. 62. - In some cases the packaging may need to contain information on both the quantity per unit volume and on the total quantity per total volume; the total quantity per total volume can be particularly important for safety reasons for medicinal products for injection and other medicinal products available in solution or suspension.

Art. 63. – (1) Different strengths of the same medicinal product should be expressed in the same manner: for example 250 mg, 500 mg, 750 mg, 1000 mg and NOT 1 g.

(2) Trailing zeros should not appear (2.5 mg and NOT 2.50 mg).

(3) The use of decimal points (or comma) should be avoided where these can be removed (in other words, 250 mg is acceptable whereas 0.25 g is not).

(4) For safety reasons it is important that micrograms is spelt out in full and not abbreviated.

(5) However, in certain instances where this poses a practical problem which cannot be solved by using a smaller type size then abbreviated forms may be used, if justified and if there are no safety concerns.

IV.4. Route of administration

Art. 64. – (1) This should be as registered in the summary of product characteristics (SPC) only according to the standard terms.

(2) Negative statements should not be used: for example "Not for intravenous use".

(3) In addition, there is a list of other non-standard abbreviations published on the EMEA website (http://www.emea.europa.eu/htms/human/qrd/docs/listnonstandard.pdf).

(5) Other non-standard routes of administration should be spelled out in full.

(6) Some routes of administration will be unfamiliar to patients and may need to be explained within the package leaflet; this is particularly important when medicinal products are made available for self-medication.

IV.5. Design and layout

Art. 65. – (1) Applicants and marketing authorisation holders should make best use of the space available to ensure that the important information is clearly mentioned on prime spaces on the outer and immediate packaging, presented in a sufficiently large type size.

(2) Company logos and pictograms (if accepted in accordance with Article 772 of Law No. 95/2006, transposing Art. 62 of Directive 2001/83/EC) may be presented, where space permits, on the outer packaging and on immediate packaging, provided they do not interfere with the legibility of the mandatory information.

Art. 66. – (1) Use of a large type size will be appropriate, although other factors may also be important in making the information legible.

(2) Consideration should be given to the line-spacing and use of white space to enhance the legibility of the information provided on the packaging.

(3) For some small packs it may not be possible to present all the critical information in the same field of view, therefore the use of any innovative

technique in packaging design to aid in the identification and selection of the medicinal products is encouraged; it is also encouraged where space is limited.

Art. 67. – (1) Colours should be chosen to ensure a good contrast between the text and the background to assure maximum legibility and accessibility of the information.

(2) Highly glossy, metallic or reflective packaging should be avoided, as this affects the legibility of the information.

(3) Different colours in the name of the product are discouraged since they may negatively impact on the correct identification of the product name.

(4) The use of different colours to distinguish different strengths of a medicinal product is strongly recommended.

Art. 68. – (1) Similarity in packaging which contributes to medication error can be reduced by the judicious use of colour on the pack.

(2) The number of colours used on packs will need careful consideration as too many colours could confuse.

(3) Where colour is used on the outer pack it is recommended that it is carried onto primary packaging to aid identification of the medicinal product.

Art. 69. - Where a multi-lingual outer and/or immediate packaging is proposed there should be a clear demarcation between different languages where space permits.

Art. 70. - All outer packaging must include space for the prescribed dose to be indicated and/or "blue box" information as required by Romania (see section IV.7.).

IV.6. Templates for labelling

Art. 71. - The European template in Romanian, approved through Minister of Public Health Order No. 399/2006, published on the NMA website, http://www.anm.ro, transposition of the model of the centralized procedure, published on the EMEA Website http://www.emea.eu.int/htms/human/qrd/qrdtemplate.htm reflects the particulars which must appear on the labelling and package leaflet of medicinal products according to Directive 2001/83/EC.

Art. 72. - For the purpose of regulatory submissions to national competent authority, the NMA, the text version of the product information is to be presented in the mandatory format and lay-out (see "QRD convention" on the EMEA Website at http://www.emea.europa.eu/htms/human/qrd/qrdplt/qrdconvention.pdf) using the electronic product information templates.

Art. 73. - When using these templates, reference should be made to relevant Community Guidelines, QRD Guidance and the "Annotated QRD Template", providing detailed guidance on how to complete each section and which can be found on the EMEA Website (http://www.emea.europa.eu/htms/human/qrd/qrdplt/AnnotatedTemplate-H.pdf) and the Heads of Agencies Website (http://www.hma.eu/uploads/media/QRD_annotated_template_CMDh.pdf).

Art. 74. - Having used the templates provided, marketing authorisation applicants/holders will still need to format the resulting text into the relevant full colour mock-ups and specimens of the packaging.

IV.7. Other information

Art. 75. – (1) As foreseen by Art. 2 of the Guideline on information specific to Romania which must appear in the "Blue Box" on the secondary package of medicinal products for human use authorised through the centralised procedure, approved through SCD No. 7/29.02.2008, Guideline transposing provisions of Art. 57 of the updated Directive 2001/83/EC, a Member State may ask for additional information to appear on the packaging concerning identification and authenticity of the medicinal products, the legal category for supply and the price.

(2) National rules will apply in these circumstances and details on the requirements for the "blue box" in mutual recognition and decentralised procedures are given in the Notice to Applicants, Volume 2A, chapter 7.

IV. 8. Blister pack presentations

Art. 76. – (1) For blister pack presentations it is important that the particulars remain available to the user up to the point at which the last dose is removed.

(2) Often it will not be possible to apply all the information over each blister pocket, consequently where a random display of the information is proposed it should frequently appear across the pack.

(3) In all cases it will be acceptable to apply the batch number and expiry date to the end of the blister strip; if technically possible, applying this information to both ends of each strip should be considered.

(4) Where a unit-dose blister presentation is proposed all the information required for blister packs must appear on each unit dose presentation.

Art. 77. - In addition, blister foils should be printed to ensure maximum legibility of the information using a sufficiently large font.

Art. 78. – (1) Colour for the text and the font style, should be chosen carefully as the legibility of the text on the foil is already impaired due to the nature of the material.

(2) Whenever possible, non-reflective material or coloured foils should be considered to enhance the readability of the information presented and the correct identification of the medicinal product.

IV. 9. Small containers

Art. 79. – (1) Where the labelling particulars set out in article 763 of law no. 95/2006, transposing Art. 54 of Directive 2001/83/EC cannot be applied in full to the labelling of small containers as a minimum the particulars set out in Art. 764 (3) transposing Art. 55(3) of the directive should be applied.

(2) Other information required in Article 763 may be added as appropriate, where space permits.

(3) The criteria for small container status would normally apply to containers of nominal capacity of 10ml or less.

(4) However, other factors may need to be taken into account such as the amount of information which has to be included and the font size necessary to ensure the legibility of the information.

Art. 80. – (1) Innovative pack design is encouraged where space is at a premium (e.g. the use of wraparound or concertina labels).

(2) Paper labels are recommended to increase the legibility of the information applied to, as much as possible, for example, ampoules.