Patient information on medicinal products – how to make it patient-centric?

AESGP, EFPIA and Medicines for Europe Joint proposals in line with Health Literacy Principles

Introduction

Everybody knows this situation: you get a prescription for a medicine from your doctor or you follow the advice of your pharmacist and end up at home with the medicinal product, open the box, take out and unfold a very large leaflet to check the dose or look for another piece of information. As it seems an impossible task to fold it back up, you might just discard it instead.

Patients have very often repeated their request for a clear, informative package leaflet which motivates them to read it, because only if read and understood, will the information contribute to the safe and effective use of the product and have a positive impact on patients' health outcomes.

The pharmaceutical industry is often criticised for illegible incomprehensible texts, but the structure and content of these patient information leaflets is highly regulated – Europe-wide.

The purpose of the package leaflet is to provide patients with information on the safe and effective use of the medicine and enable appropriate use. To ensure this, readability testing has been in place for some decades now. This being said, many improvements can be made to ensure the package leaflet is more patient-friendly, patient-relevant and accessible. The Working Group (WG) Content of the Inter-Association Task Force (IATF) on electronic product information took into account the views of patients/users and user testing companies' experience combined with research activities of the user testing companies as basis for its recommendations to improve the content, structure, and readability of patient information. The result is a set of proposals to improve the package leaflet by taking a patient-centric view.

From a broader perspective, 'information is a cornerstone of patient empowerment that enables health literacy, shared decision-making, and effective self-management' (1). Leaflets should particularly serve the needs of people with low health literacy in Europe so that they can have the appropriate health outcome in the end. By adjusting the text to these lower literacy levels, leaflets can contribute to medication literacy.

This document focuses only on the package leaflet aimed at patients; it does not provide recommendations on the summary of products characteristics (SmPC) or on the packaging such as the box the medicine is provided in.

(1) EMPATHiE, 2014

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Why is improving the package leaflet content less easy than it may seem?

Every medicine approved in the EU must have a package leaflet that has been reviewed and approved by competent authorities unless all information required is directly conveyed in the labelling (2). The order and sections of the package leaflet are imposed by the legislation and the content needs to be fully consistent with the Summary of Product Characteristics (3) which is the information for health care professionals (doctors, pharmacists, etc.). To ensure that the leaflet content is written in a language that is understandable by lay-people, package leaflets have to be 'user tested' to ensure that they are legible, clear, and easy to use (4).

In addition to the legislative requirements, several guidance documents (5) have been developed; these should be followed when drafting the leaflet.

Finally, a dedicated group at the EMA (European Medicines Agency) is asked to ensure the product information is easy to understand and clear. This group – called the Quality Review of Documents (QRD – which is composed of representatives of national medicines agencies) has also published documents to aid authorities and industry. The non-standard abbreviations and the use of terms are some of them; the most known one is the QRD template which provides guidance on how to present the product information (i.e., the SmPC, Labelling and Package Leaflet) of a medicinal product.

Despite these efforts and guidelines, reports on the content of the leaflet produced by Nivel (Netherlands Institute for Health Services Research) and the University of Leeds in 2014 (PIL-S and PILS-BOX) upon request from the European Commission highlighted a great number of shortcomings.

Amongst other recommendations, they suggested to:

- Revise the existing guidelines, in particular the **Readability Guideline, the Packaging Information Guideline.**
- Allow **more flexibility** in the information recommended in the QRD template, as long as the relevant legislation allows it.
- Improve the **input from patients during the leaflet creation process and the related methodology**.
- Publish best practice examples.
- Explore the use of **electronic media**.

In November 2017, the EMA issued an ambitious action plan (6) modelled after the European Commission's recommendations. However due to the resources available, the Agency chose to focus on the development of key principles for electronic product information (ePI), also a priority for the industry.

Nevertheless, it is key to work in parallel on the content shortcomings and take a holistic approach to achieve an improvement to patient information.

(2) Article 58 of Directive 20001/83/EC

(3) Article 59 of Directive 2001/83/EC

(4) Article 59(3) of Directive 2001/83/EC

(5) The Guideline on the packaging information develops some of the provisions mentioned in the Directive 2001/83/EC to assist in particular, when drawing up the package leaflet text. The Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use aims to assist pharmaceutical industry in how to present the package leaflets in an easy-to-understand and patient-friendly way, so it can be understood by those who receive it so they can use their medicinal product safely and appropriately. The guideline also includes guidance on consultations with target patient groups ("user tests").

(6) EMA action plan related to the European Commission's recommendations on product information: https://www.ema.europa.eu/en/documents/other/european-medicines-agency-action-plan-related-european-commissions-recommendations-product_en.pdf

As industry WG content, what have we accomplished?

To capture the unique users' perspective on the current paper package leaflets, experts from the WG Content of the IATF decided to engage with patients, carers, patients' association representatives and user testing companies. The feedback was collected from written consultation and individual interviews and in-depth workshops.

Views of patients and carers

Two workshops took place with volunteering patients and senior citizens, in December 2020 in Germany and in June 2021 in France.

All insight and feedback provided were quite consistent and highlighted similar shortcomings across patients and countries. The main complaints touched upon:

- Patients appreciate that the structure is the same between different medicines, however, they find it difficult to find the information they are looking for from the titles of the sections which are not always intuitive.
- The structure is not logical for them as it does not correspond to the order in which they are usually looking for the information.
- The leaflets are too long and contain many repetitions.
- It is very difficult (even impossible) to fold them back and put them in the package and therefore have them at hand when needed.
- They are often written in a small black font which deters patients from reading it.
- The balance between benefit and risk is not proportionate.
- On the risk aspects, patients find it confusing that some information is covered in the section on warnings and other information in the section on side effects.

- Patients did not find the current ranking of side effects by frequency relevant once experiencing a side effect; they would also prefer to have the side effects ranked by severity or body parts with clear instructions on what they should do in case they experience a side effect.
- Many patients underlined the issues they have with understanding the information in the leaflet, as the language is not patient-oriented and contains too many medical terms, particularly the sections on warnings and side effects. E.g., the name of the therapeutic group is not understood nor meaningful and they would instead like to know how the medicine acts in their body. The instructions given are seen as too vague in some instances and the patients do not feel the leaflet is 'talking' to them.
- Some parts of information like the manufacturing address or name of the product in other countries is of no relevance to them.

They also believe that a digital version can help address some of the shortcomings e.g., finding the information sought, highlighting the updated part of the leaflet for chronically ill patients, or having more visuals or videos. They, however, made it very clear that the digital version should not be an excuse to add more content and to leave the current leaflet unchanged without addressing the identified shortcomings.

> *One patient expressed the feeling that the leaflet is not addressing patients need, but more a legal document that exists for liability purposes.*

It is also interesting to observe that the feedback provided by the German and French groups of patients pointed out the same shortcomings and corroborated the findings presented in the Nivel PIL-S study which ran 5-6 years ago.

For more details, see Annexes 1 and 2.

Views of user testing companies

A series of interviews with several user testing companies took place between March 2022 and April 2022 to collect their feedback and experience and explore the current state of content, format and methodology of user testing, also in the context of digitalisation.

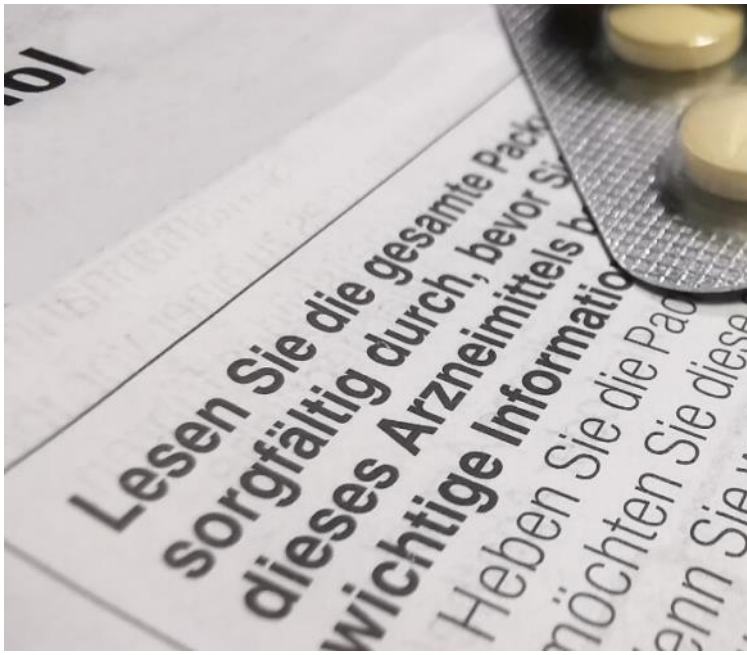
The individual feedback allowed the IATF to organise a hybrid workshop in Cambridge to discuss and refine the feedback received through the individual interviews in February 2023.

User testing companies confirmed many of the patients' concerns:

- The overall length of the leaflet was often criticised as it made navigability difficult. In addition, the length of sections or even sentences themselves were considered too long and not easy to understand.

"Increasing the number of words is a major factor in decreasing patients' motivation to read and their ability to locate the provided information; whilst also reducing trust in using the medicines."
Fuchs et al, 2012 (7)

- Repetitions such as 'talk to your doctor' could be removed and there should be more flexibility in terms of sections that could be omitted if not relevant for the patient.
- There were sometimes also multiple instances of the same issue mentioned in different sections (e.g., the sections on interactions, side effects, "use in children") which also should be avoided and thereby could contribute to a shorter leaflet.
- Also, some sections are of no use to patients. For example, looking at manufacturing details or the name of the medicinal product in other countries.
- The shortening of the whole leaflet is seen as the main priority. One user testing company successfully reduced a leaflet from 800 words to 200 words without losing any important content and the shortened leaflet successfully passed testing and was liked by patients (8).
- Medical terminology is also not understood by most people. Section 2 on risks, which is usually the one being revised the most during the life cycle of medicine, is often not well understood and differentiated. Users find it particularly difficult to see the difference between contraindications and warnings, and the section on side effects was seen as difficult to handle. Only side effects that are understood by the patients or carers and on which they can act upon should be added. It was advised to omit frequencies beyond 'very rare, rare and common'.



- Some instructions on pregnancy or driving should also be made clearer.
- The layout can also aid readability and navigability with more structuring elements (bullets, boxed text, sub-heading), as well as highlighting important information with bold text and changing the layout of the leaflet to space out the information.
- With regards to the user testing methodology, the current recruitment requirements limit a diverse population from being recruited. The flexibility experienced during the COVID-19 pandemic should be maintained to get more diverse input, while acknowledging the benefit of personal interactions.

For more details, see Annex 3.

(7) (8) Fuchs, Scheunpflug, Götze, "The Influence of the European Union's QRD Template on the Use of Package Inserts Compared with a Shorter Model Template", Pharm. Ind. 74, Nr. 1 (2012): https://www.paint-consult.com/fileadmin/editorial/downloads/publikationen/PAINT-Consult_The_influence_QRD_template_shorter_model-template.pdf

Development of recommendations for the patient information structure and content

With the objective to focus on concrete solutions and proposals to improve the leaflet within the current legislative framework, a hybrid workshop with 6 user testing companies (based in the UK and in the EU) was conducted in a hybrid format in February 2023. To ensure patient centricity, the resulting proposals were reviewed by a small group of patients.

The main recommendations were to:

- Shorten the length of the package leaflet to one page, in maximum A4 format
- Focus on patient-relevant content and language patients understand (e.g., therapy goals, fact-based benefits in a non-promotional manner).
- Re-order side effects to be more actionable for patients.
- Retain flexibility with regards to QRD template (e.g., categorisation of information by adding more sub-headings).
- Avoid repetitions by addressing elements in different categories of the leaflets (e.g., pregnancy).
- Improve the overall structure including standardisation of terms.
- Increase clarity of the sections by adding bullets, diagrams, boxed text, sub-hearings, bold and italics.
- Merge sections 5 and 6.
- Separate Contraindications and Warnings to differentiate and encourage the correct action (i.e., use different sub-headings).
- Omit manufacturing details
- Omit name of medicinal products in other countries
- Omit introductory section.
- Use 'ask your doctor' only when really needed and when it makes sense for the patient.

For detailed recommendations, see Annex 4.

The work on the QRD template should be complemented by revising the *Guideline on the readability of the labelling and package leaflet of medicinal products for human use* to convey the recommendations for a better layout. The guidance itself should be simplified and its navigability improved.

The following topics should be considered for revision in particular:

- Improve the structure and content display of the "Readability guideline" and QRD templates notably by regrouping all the various requirements in a checklist format and "Empty" QRD templates in a semi-structured format (e.g., XML) allowing flexibility, e.g. on optional sections as for special patient groups).
- Provide guidance on layout taking into consideration principles of good information design with examples.
- Provide access to documents relevant in the context of QRD, plain or lay-term language.
- Describe standards (layout) for electronic leaflet in a separate section.
- Revise section for user testing, taking into consideration feedback from user testing companies and patient associations.
- Introduce a separate section for translation rules (e.g., high level guidance on principles of faithful translation).

For detailed recommendations, see Annex 5.

Key conclusions/Recommendations - What have we learnt?

To address the shortcomings highlighted by the NIVEL report which were echoed and repeated by patients, carers and user testing companies, and taking a patient -centric perspective on the leaflet, we recommend:

- A clear, informative package leaflet that motivates patients to read has a better chance of leading to correct patient behaviour.
- Clarity and patient-relevant content in a shorter format is crucial.
- The content of the leaflet needs to be amended through legislation (e.g. notably moving the more detailed requirements of the leaflet content to an annex to ease update) but mostly through non-legislative documents.
- Guideline concept for Readability is to be created to keep all related guidance documents together.
- User testing method improvements are to be implemented.
- Improvement opportunities regarding the provision of information should focus on patient-relevant content, reduced text volume and increased clarity e.g., by using clear language.
- A clearer structure and the use of sub-headings and bullet points with a clear and succinct layout are also key to increase readability.
- Avoiding repetitive statements especially when information conflicts in different sections is also recommended.
- Inclusion of visual aids could allow more ease of reading by breaking up the text.

Looking forward, digitalisation will offer, amongst many other features, enhanced accessibility, up to date information, searchability and, customization options. When combined with clear, optimised leaflet content, it will ensure that product information is patient-centric thereby improving medication literacy and compliance.

Patient Information on Medicinal Product – how to improve
Guiding principles for patient-centric leaflets

- Only package leaflets that are read and understood by patients and carers can contribute to the appropriate, safe and effective use of medicines and ultimately have a positive impact on health outcomes.
- Our proposals are based on literature, interactions with patients and user testing companies are in line with Health and medication Literacy Principles.
- Shortening the length of the package leaflet should be done by focusing on patient-relevant content.
- By applying good information design principles, using plain language and relying on patient-centricity the clarity and structure of leaflets will be improved.
- Specific and detailed proposals are made for each section.
- Comprehensive and simplified guidance needed to reflect all of the above to allow for consistent implementation

Patient information on medicinal products – how to make it patient-centric? Annexes

List of Annexes

- **Annex 1:** IATF (Inter Association Task Force) Patient Workshop (Pilot Germany, December 2020)
- **Annex 2:** Patient&Carer Workshop with the French Skin Federation (June 2021)
- **Annex 3:** Interviews with user testing companies (March/April 2022)
- **Annex 4:** Workshop in February 2023 and refinement for QRD / Industry Meeting in May 2023
- **Annex 5:** IATF Position paper on updating of readability guideline

Annex 1

IATF (Inter Association Task Force) Patient Workshop run in Germany on 4th December 2020 on the Readability and comprehensibility of patient information leaflets (PIL) of medicinal products

General Problems

- Only few patients read the PIL, and if so - not necessarily the whole text:
- Problems with structure
- Problems with text comprehensibility
- Problems with amount of text
- Problems with layout
- Problems are additionally increased by pain points in health care systems
- Frequent drug substitution (with different information in the PILs for the same active substance)
- Insufficient explanation of physician / pharmacist (lack of time, incomprehensible, is forgotten quickly)
- Use of many medicinal products
- Insufficient medication plan – no interaction check, not accessible for patients
- Trustful sources of information not known

Can patients find necessary information in the PIL?

- Normally, patients look for the dosage instructions to begin with (which are placed quite at the end of the text)
- Positive aspect – the PIL structure is always the same – it should remain the same for all sorts of medicinal products
- Chronically ill/ multimorbid patients often are somewhat more familiar with the structure

Problems with the structure and the ease of finding information

- Structure and logical setup are not known and cannot be recognised clearly
- Structure is not distinctive, not recognisable, not consistent
- Headings are not phrased in a comprehensible way and the layout does not display them clearly as such
- Poor layout (no prominent formatting)
- Structure is not logical – some aspects are covered in warnings, others in interactions, others in side effects – the context is missing
- Large amount of text has negative implications on comprehensibility and readability
- Thin paper (transparent paper and print on both sides makes text illegible)
- Fonts are too small
- Digital version may offer a better visibility of the structure
- Layout can be improved by clear distinctive features for structure (bolding, underlining, paragraphs)

Understanding the Text – no Chance?

- Many patients have problems to understand the information in the PIL
- The language is not patient-oriented
- The texts contain too many technical/medical/ foreign terms
- Especially the sections with warnings and side effects are difficult to understand
- The sentences are too long
- The style is too static – too many nouns
- The patients are not consistently addressed directly
- The instructions are vague or unclear (e. g. the driving warnings)
- To some extent understood easier (but hard to find):
- Dosage instructions (table would be welcome)
- Caveat: different display of amounts of active ingredients / doses! (Example: salt or hydrate of active ingredients resulting in differences in amount. Dosing in dosage instructions may be perceived as „varying“ ➔ standardisation of the description of the active ingredient?)

Improving the Comprehensibility of Texts

- PILs should be “translated“ to an easily comprehensible language based on the rules for:
- Easy language – for everybody – more comprehensible than complex text
- Simple language – for persons with cognitive restrictions – follows special rules
- They should be displayed barrier free (Request of the European Accessibility Act (EU-Richtlinie 2019/882) and Inclusion)
- Examples and information (German websites selection):
    - https://www.leichte-sprache.org/
    - http://www.bmas.de/SharedDocs/Downloads/DE/PDF-Publikationen/a752-ratgeber-leichte-sprache.pdf?__blob=publicationFile
    - https://www.inform-lebenshilfe.de/inform/veranstaltungen/termine/bv/200802-bv-leichte-sprache-reihe-ber.php
    - https://www.aktion-mensch.de/dafuer-stehen-wir/das-bewirken-wir/menschen-magazin/einfache-sprache.html
    - https://www.g-ba.de/leichte-sprache/uebersicht/

Content of the PIL

- The text is too long
- The following information is relevant for the patients:
  - Dosage
  - Warnings
  - Side effects
  - Interactions
  - Ingredients
- Superfluous: addresses/ product names from other countries
- Missing nevertheless:
  - Information on the relation between benefits and risks
  - Benefit: What does the product do within my body?
  - Risk in % (for the frequency of side effects)
- For chronically ill patients: indicating/flagging updated or new information

Representation of Side Effects as well as Warnings and Contraindications

- Different side effects for the same active substance are confusing
- Please see also frequent product substitution
- Too long, too detailed
- Description [of the same event] in various sections is unfavourable (perceived as repetition, confusing)
- Improvement could be:
  - Representation according organ systems
  - Patients who tend for example to stomach problems could search specifically
  - Listing the most frequent side effects
  - Listing serious side effects together with clear instructions on how to react
- Is a dissociation from liability law possible? (legal protections may cause long texts)

Layout: Important elements for the design

- Font size
- Format – easily to be folded and stored
- Paper – not too thin nor transparent
- Use of more structural elements
- Use of pictograms as signposts – known to everybody
- More use of colours or text formatting while considering readability for persons with impaired vision

Digital Version

- Can assist orientation/overview
- Table of contents
- Updates can be made easier/faster accessible and better visible/flagged
- BUT:
- No excuse for adding even more content – „long“ texts (definition?) are asked to be shortened
- **Cannot** mitigate content related deficiencies
- Videos and visualisations are required
- Alternative options for design should be explored
- Summary (simple patient-friendly language) combined with linked detailed information (easy language including medical data) instead of patient information plus specialist information as alter ego (separate documents) with similar content
- **All Options should be well considered and used deliberately!**
- Audience is aware of German Pilot GI 4.0

PIL for Everybody?

- THE PATIENT does not exist!!
- Different requirements of various and diverse patient groups (age, education, frequency/number of diseases etc.)
- Comprehensibility should be adapted to those with most difficulties in understanding
- **PILs should be comprehensible for all patients and agreeable in length!**
- Short summary with key points in the pack is desirable – with reference to additional information (SmPC – contact point of company – also for laymen)
- It is difficult to define important content for a summary, therefore guidance can be:
- What do patients read – dosage instructions
- What is important from the view of drug safety – to report any problems / discomfort
- Affected patients should be included in the PIL creation!
- **Everybody participating in the creation of PILs should always consider the target audience in the first place, that means patients or their caregivers!**

Written feedback from the questionnaire

- Consistent with the feedback provided during the workshop
- Confirmed that patients **do** read the leaflet
- Leaflet is much more comprehensive than information provided by HCPs to patients
- Unbalance felt between benefit and warnings/side effects
- one patient illustrated it by measuring the length of the sections!
- Compared to choosing Charybdis or Scylla - suffering either from side effects or from the disease not getting treated
- Feeling that the leaflet is not addressing patients (even less female patients), but more a legal document

Annex 2

Patient & Carer Workshop with the French Skin Federation held on 17 June 2021

Patient associations: French Skin Federation, Cutis Laxa Association and Ichtioze France Association.
Answers were consistent on many aspects with the German patients interview.
New/additional elements are presented below.

Content

- No hook for leaflet reading
- **Too much text**
- Improve use of visuals and tables (posology, method of administration)
- **Missing information : what is the benefit of taking the medicine ?**
- What does the product do within my body? Lay language description of the mechanism of action (cf activity of the molecule/class of molecules).
- B/R unbalanced presentation ⇨ Be clearer on the B/R
- Risk of NOT TAKING the medicine is missing
- **Missing information - general**
- Which interactions are to be described in the leaflet? How to express Interactions in lay language so that patients can act upon them, particularly for non-prescription medicines where there may be no interface with a healthcare professional.

Key information

- Indication
- Contraindication
- Dosage/Method of administration
- Undesirable effects (the most frequent or more serious cases + description of symptoms and what the patient should do in case of symptoms)

Layout

- Number of folds has a negative impact on the readability, handling and re-use. The difficulty to refold is proportionate to the length of the leaflet and often the leaflet is discarded.
- Colour could improve readability (enhance PL structure)

Annex 3

Interviews with user testing companies in March-April 2022 - Compilation of feedbacks received

Most frequently revised sections in PIL following user testing

Section 2 is the section which is most frequently changed following user testing

- Not optimal in terms of heading/sub-heading structure
- Pregnancy wording often not precise or contradictory ('Do not take…' vers 'Consult with your doctor' (QRD))
- Adding references from section 2 to section 4 (or vice versa)

Section 3

- Adding sub-headings

What could be improved

- Shorten the whole PIL (by far the most important issue)
- shorten long text passages
- One page leaflet
- Sufficiently large font size
- More flexibility in regards to QRD (e.g. categorisation of information by adding more sub-headings)
- More use of structuring elements (especially for long text passages)
    - bullet points
    - diagrams
    - boxed text
    - sub-headings
- Using bold or italics for relevant information
- 2-column format rather than 1-column format
- Including sub-headings also in the table of content at the beginning
- Sub-headings not directly below heading (could easily be overlooked)
- Avoid ambiguity by simplifying especially **sections 2** and **4**
- Use of alcohol/driving warning
    - Use of standard warnings instead of "Do not drink…" if not contra-indicated
    - 'it is not recommended…' is confusing à better: 'talk to your doctor'
- Pregnancy/Breastfeeding: Only clear statement whether allowed or not, otherwise 'Talk to your doctor'
- List of side effects is often too long and scares off the patients: Name (only) side effects which the patient can influence
- Use more layman-friendly terminology
- Avoiding multiple mentions of the same issue in different sections (e.g. interactions, side effects, "use in children")
- Merging **sections 5** and **6**
- Landscape rather the portrait format

What / which section(s) could be omitted / are less important

- Administrative information
    - Manufacturer (**section 6**)
    - Addresses of MAH (**section 6**) ➔ website
- List of names of medicinal product in other EU countries (section 6)
- Introduction at the beginning 'Read all of this leaflet carefully…'
- Combining double information
    - "use in children" (sections 2 and 3)
- 'Ask your doctor or pharmacist' only once
- **Section 4:** Omit frequencies behind 'common, rare, very rare'

Annex 4

Workshop in February 2023 and refinement for QRD / Industry Meeting in May 2023

Detailed Recommendations:

- Proposals for improvements to the Package Leaflet – For discussion
- Word Template Considerations

Formatting

- Consider using a sans serif font for the QRD word Template published on the EMA Website

Style

- **Use headings** style formatting for outline of structure in the QRD word template for better overview
- Proposals to shorten the length of the Package Leaflet

Shorten standard statements to 20 words max.

- Already successfully piloted

Make some sections optional, as relevant:

- Patient groups (e.g., Pregnancy)
- Presentations of medicinal product
- Combination products (i.e., medicine and device) need extra section for IFU e.g., section 7

Avoid repetitions e.g., "contact your doctor/Health care professional"

- Be more selective with referral to the HCP
- "signpost" where possible to trusted sources via e.g., QR code or a URL
- Omit content relevant to HCP only, e.g., HCP IFU provision via electronic version

Proposals for Clarity and Structure

Introductory paragraph

- Consider omitting completely – for prescription medicines, statement that product should not be passed on to others could be placed in Section 1 (research based).

Instructions for use

- Introduction of an optional chapter to explain use of device where applicable. When these instructions are quite long, a separate section at the end or a separate leaflet / brochure is better than inclusion in the dosage section. In case these instructions are included as a special section of the PIL, this section should be included in the Table of contents.

Table of content/structure

- Section 2 is perceived as too long – therefore it should be split.
- Contraindications (heading needs to be phrased in lay terms) and the rest of the warnings should be separated, also in view that most patients do not understand or recognise the difference as it is not clear that a difference exists between contra-indications and warnings.

Should allow inclusion of optional sub-headings

- Consider re-phrasing headings and testing them with support of the user testing companies.
- Consider recommending that Table of Contents could become optional as showing the key points of the sections with links/references to complete section – see also Australian example of CMI. Only for digital version and with disclaimer.
- Using pictograms as a signpost – might be based on MEB experience (difficult, colours not always possible for printed leaflets). Selection of EU harmonised pictograms to be used consistently – existing pictograms (Vet legislation to be considered and misinterpretations of symbol meaning due to cultural difference to be avoided).
- **Example of CMI**
- Template for a one-page summary for digital versions
- References/links to the complete text
- Easy to follow links in digital version

Contents

- Disclaimer
- Indication
- Contraindication
- Interactions

- Dosage/use Instructions
- Warnings
- Side effects

Proposals for Indication Section

Information on Benefit

- Patients want to see the benefits explained to them
- Most leaflets are perceived as too risk-based – consider the recommendation that information on benefits should also include the risk of not being treated. However, the emphasis on the risks involved in taking the medicine must not unsettle the patient in such a way that they do not take the medicine and thus expose themselves to an even greater risk of not having their condition treated.
- Therapy goals should be explained in patient-friendly terms only. Examples are useful e.g. is it treatment of symptoms or prevention of recurrence of an underlying disease?
- It should not be promotional.

Information on disease and medicine

- **Consider not including information on pharmacotherapeutic group, but only necessary information,** bearing in mind that more information might be needed for non-prescription medicines.
- Drug class in patient friendly terms can be important in some cases- so that patients can ascertain if they would have drug interactions with any other medicine they may have to take, but too much theoretical information needs to be avoided. Different patients may have different needs.

Mode of action

- The information on how medication works may be important if there is a consequence for the patient (e.g. biologics suppressing immune reactions). However, if mode of action is not relevant, then it is recommended to leave it out.

Proposals for Dosage Section

Units

- Doses should be expressed primarily, in units that are available for the patient, e.g. as tablet counts etc. (also research based)

Structure

- Sub-headings for different patient groups or formulations/strengths should be recommended.

Use of bulleted lists

- Use of bulleted lists is preferable or simple tables can be of help.

HCP administration

- In this case no detailed information should be given, just a statement that the patient will receive the product from a HCP. The information should be accessible via links/official repository in the SmPC or if really needed placed at the end in a separate section for HCPs.

Information on Medical Devices

- Depending on length of information, this information can be included directly or an additional optional section at the end or a separate leaflet/ brochure should be considered. Patients want to use it to follow it stepwise – especially if not used daily. Visuals are very welcome - to be integrated in the text (to allow easy transformation in hearing version).

Proposals for Warnings Section

Split this section in 2 parts

- Contraindications and warnings and precautions should be separated into 2 main sections to allow the patients to understand the distinction and also facilitate the ease of finding information.
- Note: Wording of headings needs to be patient-friendly.

Class effects

- Consider side effects only for the specific section 4 (or to be re-numbered). Here only real “class warnings” should be applicable.

Pregnancy/Lactation Statements

- Recommendations in the annotated template should emphasise optionality of statements and the need to select stronger wording for a contraindication, as needed. Standard statements to select from, as we have for the SmPC.

Proposals for Side Effects

Frequency definitions

- Consider how frequency is described in the template.

- Discussion at Workshop that frequency descriptions / definitions are not well understood. Some patients would prefer an order according to body part or severity. Frequency definitions are generally overestimated by lay people, and this can raise unnecessary concern.

Ordering of Side Effects

- Consider ordering side effects according to relevance for the patient (severity, frequency) and according to recommended actions.
- Australian CMI example which is seen as useful by patients – specific subheadings could be introduced to make this visible.
- Information should not only be readable but actionable for the patients.

Umbrella terms

- Use of umbrella terms should be encouraged rather than listing every single sub-term. Only if the specific term is accompanied by special instructions, it might be needed.

Laboratory Values

- Consider recommendation to explain only that the HCP might want to carry out laboratory tests as a general statement rather than listing all values, e.g. “Your doctor may test for …”. Should perhaps come under separate sub-heading. Where side effects don’t have an obvious symptom, but patients need to be aware, make this clear.

Detailed information

- Links or references to more detailed information of SmPC / EPAR or other trusted source could help. – not only EMA sources, but national trusted sources as well)

Glossary

- EMA Glossary should be expanded to this purpose for consistent use of patient friendly terminology

Proposals for Storage Section

Disposal Statement

- One single statement does not work EU wide due to different national provisions, propose to make reference to national/local practice/guideline/ regulation

Children warning

- The statement to keep out of sight and reach of children is a repetition from the outer pack / carton. Consider removing it.

Recommendation Other Information Section

These are currently in the legislation, and could be for a future edit as have limited patient value

Contact point

- Manufacturer, Pharmaceutical Company, and local representative – too many to select for patients only one address with the relevant communication channels (telephone, e-mail)– still within legislation, but consider giving only one point of contact (rest is clear by batch information if needed) – delete MAH and manufacturer.

Mutual Recognition Procedure

- Consider omitting list of approved product names in the EU. It is not useful, approved does not mean marketed, and by active ingredient the product can be identified in any pharmacy EU-wide.

Pack sizes

- Information could be removed, as it is on the outer package – might not be within the legislation.

Proposals on Testing Method

Acceptance of user testing

- Test results should be respected and tested language should not be changed (without good reason) by assessors.

Timing

- As late in the procedure as possible, to ensure the version tested is close to final, including accelerated procedures.

Demographics

- Flexibility in the testing method to allow f2f and virtual settings helps to recruit a wider diversity of testing population, both on location and demographics.

References - Annex 4

- *Pil_s NIVEL study – July 2014*
- *Pilbox NIVEL study – July 2014*
- *NIVEL considerations – EU Commission (21 Oct 2015)*
- *European Medicines Agency, Product-information templates - Human, QRD annotated template: https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/product-information/product-information-templates-human#centralised-procedures---quality-review-of-documents-(qrd)-templates-section*
- *A. Wolf, J. Fuchs, H. G. Schweim, "QRD Template Texts Intended for Package Inserts, Development from the first QRD template up to the new draft of July 2012": https://www.paint-consult.com/fileadmin/editorial/downloads/publikationen/PAINT-Consult_QRD_template_development.pdf*
- *J. Fuchs, C. Scheunpflug, E. A. Götze, "The Influence of the European Union's QRD Template on the Use of Package Inserts Compared with a Shorter Model Template": https://www.paint-consult.com/fileadmin/editorial/downloads/publikationen/PAINT-Consult_The_influence_QRD_template_shorter_model-template.pdf*
- *A. Wolf, J. Fuchs, H. G. Schweim, "Readability of the European QRD Template, The European QRD template version 8 in comparison to its predecessor and a shorter model template": https://www.paint-consult.com/fileadmin/editorial/downloads/publikationen/PAINT-Consult_Readability_European_QRD_Template.pdf*
- *Dr. J. Fuchs, S. Banow, N. Görbert, and PD M. Hippius, "Importance of Package Insert Information in the European Union, Medicinal and pharmaceutical experts questioning results": https://www.paint-consult.com/fileadmin/editorial/downloads/publikationen/PAINT-Consult_importance_package_insert_EU.pdf*
- *Cross-Over-readability-test-study of five original and five model package leaflets, n = 1105 participants - see Fuchs, Hippius Inappropriate dosage instructions - PAINT1 study article PEC 2007.7*
- *TGA Product and Consumer Medicine Information Licence, https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2022-CMI-02443-1*
- *The Better Use programme | Our tasks | Medicines Evaluation Board (cbg-meb.nl): https://english.cbg-meb.nl/topics/about-meb-our-tasks/about-meb-better-use-of-medicines/the-better-use-programme*

Annex 5

Position Paper on updating the Guideline on the readability of the labelling and package leaflet of medicinal products for human use, Revision 1, January 2009

Background

Following the publication of the EC assessment report identifying current shortcomings in the product information texts of medicinal products, EMA further outlined specific objectives concerning (amongst others) "amendments of guidelines and Quality Review Documents (QRD) templates to enhance readability of package leaflets" in their action plan. One of the proposed actions is to revise the Guideline on the readability of the labelling and package leaflet of medicinal products for human use, Revision 1, January 2009 (mentioned as "Readability Guideline" in the rest of this document) in terms of language and to include principles of good information design and layout.

Position statement

The revision of the "Readability Guideline" is considered an important action. Particularly as 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 medicine safely and appropriately". This 'understanding' of the information should not be under estimated as it could subsequently result in better adherence and eventually better health outcomes. Additionally, the guideline includes guidance on how to consult with target patient groups for the printed package leaflet.

According to the Study on the Package Leaflets and the Summaries of Product Characteristics of Medicinal Products for Human use (PIL-S-study), the current guidelines are considered not to be clear in several aspects, for example:

- font sizes
- line spacing
- lack of detail on the principles of good information design in which content and layout are jointly considered
- too restrictive in some respects

On the other hand, more flexibility is needed as medicines and contexts may differ.

Our proposal is not only to update the advice given in this guideline but also to revise its structure. Indeed, the "Readability guideline" is a part of a complex compilation of guidelines, appendices, templates, and other decisions which all concern product information. This compilation is difficult to use as the information is scattered and not always consistent across the various documents Within the readability guideline itself the topics are very mixed and scattered, e.g. as how to phrase and how to put it into layout, regarding the label or the leaflet.

The following topics should be considered for revision in particular:

Structure and content display of the Readability guideline and QRD templates

- The clarity of the "Readability guideline" could be significantly improved by a layout change e.g. regroup all the various requirements in a checklist format (see annex) instead of lengthy paragraphs.
- "Empty" QRD templates preferable already in a semi-structured format rather than Word allowing flexibility, e.g. on optional sections as for special patient groups.

Patient Information leaflet guidance on layout

- Overall, the layout rules provided in the readability guideline should follow the principles of good information design.
- The guidance should reflect principles rather than strict rules.
- Guidance for the leaflets as paper and electronic versions should be provided.
- The guidance should also take into account leaflets for small containers and multiple language presentations.
- Good examples of information design should be shared by agencies or link to respective websites (e.g. PIL of the month (MHRA)).
- QRD template should allow more flexibility regarding layout (e.g. block headings, colours, bold printing etc.).

Patient information leaflet guidance on content and format

- Guidance on wording for patient-friendly lay-terms for medical terms on indications, side effects as well as special patient groups or carers. E.g. creation of a dictionary/translation memory. At a starting point this could be based on the already existing documents from UK (*Layterms UK 2*) or EMA (*EMA Medical terms simplifier*). The guidance should be based on health literacy principles (link to literature).
- Accessibility of the leaflet which needs to be provided e.g. in formats suitable for partially-sighted people or in formats perceptible by hearing for blind persons – considering also other constraints which might e.g. be solved by barrier free technology possible for electronic versions.
- Easy access to a list of the relevant documents from EMA, CMDh with regard to format, conventions, stylistic standards (e.g. EMA/25090/2002 rev.19: Compilation of QRD decisions…, etc.).

Standards for electronic leaflets – a separate section in the "Readability Guideline" should outline standards to guarantee the readability of the electronic version (content being the same approved text as in the paper leaflet).

- User-friendly electronic format
    - Barrier-free technology – use of reading device/screen readers
    - Better overview – easy navigation – allowing easy access to the preferred level of information - tailoring for decision-making by patients and HCPs
    - Search function
    - Scalable font size/amenable to other formats
    - Use of videos (as part of an educational material)
    - Hover-over glossary (but text should be understandable without need of glossary whenever possible)
    - Multilingual versions
    - Communication about changes
    - Direct link to the respective national reporting system for adverse reactions
- Digital product information system – unbiased official trusted source
- Validated system, authority approved information – interoperability for integration in eHealth/e-prescription systems
- Real-time information, widely available – accessible from computers and mobile phones – for patient without these devices with the option to obtain the Patient Information e.g. at the point of sales via print-out or other suitable technologies

User testing

- The advice is to strengthen input from patients, patient organisations and experience from companies specialised on readability testing and to make testing more iterative and interactive, whilst working in a streamlined way that facilitates input but does not add unnecessary burdensome processes.
- User testing results should always have higher priority in comparison to QRD template (formatting) requirements.
- Testing of non-standard types of application by human factors testing (e.g. correct use of pen, syringe, inhaler etc.) should be considered
- Testing of electronic version: No additional test should be performed on electronic PI content. The proposed standard should be created and tested against paper in a pilot– this test would establish the standard for ePI and by adhering to this, content test on paper would be sufficient. The proposed standard could be evaluated in a test study – e.g. parallel user testing of the same text in paper and electronic version of a certain number of leaflets. The aim would be to achieve at least the same level of understanding.
- User testing can be performed in any EEA language – translation standards should be implemented in order to guarantee the quality (i.e. patient-friendly) of the translations. (See below section e) 'Translation')
- Guidance should be provided in case of applications with expedited timelines
- Addition of a link in section 4.2 on guideline regarding bridging: "QRD form for submission and assessment of user testing bridging proposals" (EMA/355722/2014 - Rev.1)
- Compiling feedback from user tests to be considered, i.e. preparing of a respective document which will be available publicly to share best practices.

Packaging information (except leaflet – e. g here already exists a separate guideline)

- Recommendations for blind and partially sighted patients need to be included.
- Guidance should be provided on how to manage or split leaflets that are very long due to several languages or integrated IFUs.

Translation

- Relocate content on translations to an own section 'guideline on translation'.
- High-level guidance on principles of faithful translation incl. lay language translation should be provided.
- Clearly phrase, that lay language introduced through user testing should not get lost during translations.

General guidance on how to implement patient-friendly wording and layout in patient leaflets and packaging material

CONTENT CHECKLIST

This document summarises the European readability guideline recommendations.

Package leaflet		References
Syntax		
	Use simple words of few syllables	1
	Make short sentences (20 words maximum) and vary sentences length	1
	Use bullet points instead of long paragraphs (side effects...)	1
	Set out side effects by order of importance/ frequency and not by organ/ system/class in the PIL.	1
	Explain frequency terms in a patient-friendly wording: "very common" (more than 1 in 10 patients).	1
	Start the side effects section with the existing serious side effect when patient should take urgent action	1
Style		
	Use past tense in the SmPC and direct speech in the PIL (restart treatment instead of treatment should be restarted)	1
	Instructions to patient should come first, followed by the reasoning ("take care with X if you have asthma- it may bring on an attack")	1
	Avoid unnecessary repetition of the invented name in the PIL (use substance, pronouns, alternative terms…)	1
	Spell out the full term word once, followed by the abbreviation in brackets before using abbreviations throughout the text	1
	Do not use scientific symbols such as "<" or ">"	1
	Avoid technical/medical terms.	1
	Use lay term and/or explained medical term. Be consistent throughout the PIL	1
	Always spell out "micrograms" in full	2
Use of symbols and pictograms		
	Use clear symbols and pictograms, do not use it in case of doubt on their meaning	1
	Symbols and pictograms should not replace the actual text in the leaflet	1
Additional information		
	Use a different leaflet for each strength and form of a medicine Discuss the use of combined package leaflets on a case-by-case basis	1
	If relevant for the treatment, refer to other existing strengths and pharmaceutical forms of the same medicine in the PIL	1

Labelling (Outer carton, blister foil, label)		References
Name of the medicine		
	Use short terms for pharmaceutical forms (see EDQM Standard Terms) if no space on	1
Strength and total content		
	Express different strengths of the same medicine in the same manner (250 mg and 1000 mg and not 250 mg and 1 g)	1
	Do not use trailing zeros (2.5 mg and not 2.50 mg)	1
	Avoid the use of decimal points/ comma (250 mg and not 0.25 g)	1
	Outer carton: always spell out "micrograms" in full	1, 2
Route of administration		
	Use only standard terms/ abbreviations (i.v., i.m.…) and official non-standard abbrevia-	1
	Do not use negative statements ("not for intravenous use")	1

References - Annex 5

- *European Commission Entreprise and Industry Directorate-General, Guideline on the readability of the labelling and package leaflet of medicinal products for human use, Revision 1, 12 January 2009: https://health.ec.europa.eu/system/files/2016-11/2009_01_12_readability_guideline_final_en_0.pdf*
- *European Medicines Agency, QRD decisions on stylistic matters in product information : https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/compilation-quality-review-documents-qrd-stylistic-matters-product-information_en.pdf*

About us

The Association of the European Self-Care Industry (AESGP)
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