

# Best practice guidance on patient information leaflets (PILs)

Guidance on how to write good quality information for patients about medicines

## 1. Background

Patient information leaflets (PILs) have been a legal requirement in the UK since 1999 for all medicines. Survey findings tell us that patients want more information than they currently receive and that they value the PIL which comes with the medicine more highly than any other source of information except doctors and pharmacists. The statutory PIL is both available and authoritative and for many patients this is the only written information they will have about the medicines they are taking.

Good information helps patients to participate fully in concordant decision-making about medicines prescribed for or recommended to them by healthcare professionals. Self-care, a key government objective, relies heavily on patients having sufficient high-quality information to use in their decision-making. For medicine purchases, over-the-counter interaction between the patient and a healthcare professional may be limited or unavailable. In this case, written information has an increased importance for safe use of the medicine.

In 2005 the Medicines and Healthcare products Regulatory Agency, in conjunction with the Committee on Safety of Medicines (now the Commission on Human Medicines), published "[Always Read the Leaflet – getting the best information with every medicine](#)". (ARTL) This document is the primary source of information in relation to good practice in the area of patient information provision.

## 2. Purpose

The purpose of this guidance is to bring together all advice published by MHRA in this area and to supplement the information presented in ARTL to support a move to greater self-regulation by the pharmaceutical industry when making changes to PILs. When the guidance is applied it will ensure that the PILs available with all medicines are clear and understandable, enabling patients to act appropriately. Leaflets which follow the guidance will also reflect the views of patients as envisaged by the legislation.

Those involved in the design and drafting of PILs should ensure that the following sections and the advice in ARTL are taken into account prior to submitting PILs to the MHRA as any deviations from this guidance may need to be justified where these impact on safe use of medicines.

### 3. Scope

This is best practice guidance to be read alongside the legislative requirements which are set out in Part 13 of the [Human Medicine Regulations \(HMRs\) 2012](#). The guidance has been drafted to support the legal framework set out in national legislation and to supplement the publication ARTL. It must be taken into account by marketing authorisation holders (MAH) when preparing the leaflets accompanying licence applications and variation submissions or when submitting notifications or applications under Part 13 of the HMRs.

The guidance applies equally to prescription-only medicines and those available over –the counter. In assessing applications or when undertaking audits of notifications or in the handling of complaints about PILs, the Agency will consider patient safety in the light of experience and any adverse incidents reported.

### 4. General considerations

All patient information leaflets are required to follow the order and include the content specified in Schedule 27 to the HMRs. Combined leaflets for different strengths and/or forms of product are acceptable.

The legislation does not address issues in relation to design and layout or provide detail on how to develop patient-accessible language. The legislation is explicit in instructing applicants to ensure information design is considered along with the need for translation into all languages, including English where harmonised texts are not in good quality English. Applicants will need to refer to ARTL and this supplementary guidance in order to maximise the quality of the full colour mock-ups which will be provided to the MHRA with application and notification submissions and which will form part of the approval of the marketing authorisation (MA).

In addition to the provisions in **Schedule 27 to the HMRs** concerning content and order of the PIL the legislation also requires applicants to provide evidence that the leaflet proposed for marketing reflects the results of consultation with target patient groups. National<sup>1</sup> guidance is available concerning mechanisms for demonstrating compliance with [user testing]. General advice in this area is provided below in section 7.

### 5. Order and content of the information

#### 5.1 Order of the information

**Schedule 27 to the HMRs** sets out the six main sections of the PIL and the information which must be included within each of these sections. These are:

- **Identification of the medicine:**  
The name, the active substance(s), the pharmaceutical form, and the strength of the product should be stated.
- **Therapeutic indications:**  
The conditions for which the medicine is authorised must be listed. This section should include any benefit information considered appropriate.
- **Information necessary before taking the medicine:**  
Situations where the medicine should not be used, any precautions, warnings, interactions with other medicines or foods, information for special groups of patients (pregnant or nursing mothers), and any effects the medicine may have on the patient's ability to drive.
- **Dosage:**  
How to take or use the medicine including both the route and method of administration, how often it should be given, how long the course of treatment will last, what to do if a dose is missed and, if relevant, what to do in the event of an overdose and the risk of withdrawal effects.
- **Description of side effects:**  
All the effects which may occur under normal use of the medicine and what action the patient should take if any of these occur. These should be listed by seriousness and then by frequency.
- **Additional information:**  
This covers information on excipient details, a description of the product, registered pack sizes, storage conditions, and name and address of the MAH and manufacturer.

Although there is no need to adhere to the order of the subsections within each of these sections, MAHs will need to consider how best to set out the information required to appear. Where particular subsections of schedule 27 do not apply for a particular medicine, there is no need to include reference to this in the mock-up provided.

## **5.2 Content Regulation 260 of the HMRs**

This requires the leaflet to be drawn up in accordance with the summary of product characteristics (SmPC). How the information is worded is equally important in making sure the key messages for safe use can be understood. Before submitting your leaflet for user testing make sure you have considered the way in which the information is written and take account of best practice in this area. Your writing style should be considered in advance of submitting a leaflet for user testing in order to have the best chance of success.

The content cannot be identical to the information presented in the SmPC and will need to be translated into colloquial English for the patient. This will ensure that the resulting mock-up meets the requirement in Regulation 260 of the HMRs to be clear and understandable and to be clearly legible in the official language of the member state. For the United Kingdom the official language is English.

Translations of the PIL into other languages in common use in the United Kingdom are permitted provided that the information presented is identical in all languages. Only the English-language leaflet will be subject to approval as part of the MA.

Key points to note:

- Consistency with the SmPC and compliance with the HMR 2012 Part 13 must first be achieved (see below, Using Templates)
- Complex language and medical jargon cause difficulty in understanding by patients
- Translate all the information into lay language
- Make sure you use colloquial English (for the mock-ups of leaflets for the United Kingdom)
- Use short sentences and/or bullet points
- Many phrases can confuse so consider more colloquial terms for the United Kingdom
- Do not use the system organ class arrangement for side effects as patients are unable to follow this logic. Side effects should be grouped by seriousness to enable patients to understand when to take action and what that action should be
- Make sure risks are communicated clearly to patients. Guidance has already been published in *“Always Read the Leaflet”* and examples of best practice in this area are available. Explanations (including frequency with respect to the side effects) are known to be helpful to readers and can put the risk in context.

### **5.3 Using templates**

A template will help to make sure that the information required appears in the correct order. This will not help with design and layout, however, and once you have the text for the leaflet you will still need to make sure that the design and layout of the words produces a high quality document which patients will be able to read and understand.

You should make sure that when preparing your mock-up leaflet for testing you reword your leaflet to ensure that all the information is translated into terms which the patient can understand.

Particular care needs to be taken with the sections in the PIL covering contraindications, warnings and precautions and the side effects sections. These are often very long and written in complex language. Make sure that you have used the guidance below on design to help reduce the likelihood of problems arising in testing.

## **6. Design and layout**

A well written and clearly designed leaflet can maximise the number of people who can use the information to make decisions about their medicine so that they can use it safely and effectively.

Information design essentially makes complex information easy to use and easy to understand. It is a particularly important aspect of document development where the risk of misunderstanding is likely to come with a cost – highly likely in the field of medicines information. This is an iterative process and in deciding on a design for a particular PIL there are likely to be a number of different designs and modifications in the development process.

Many test houses will offer to review and improve the design and layout of the information in the PIL to ensure a high quality PIL is achieved and there is more chance of a successful outcome in the user test. You are advised to take advantage of these services.

### **6.1 Information Design**

Whether this is the first time you have written and designed a PIL, or even if you have some experience, you may need advice on best practice in information design. In its broadest sense information design – although a complete subject in its own right – covers the following:

#### *Information architecture*

How the information is set out in the document is an important feature of information design. It provides order and structure to the document as well as looking at navigation tools within the document. Very little information is read from beginning to end (with the exception of novels) and the way in which the information is arranged is important in ensuring that readers can find their way around it. Making the information easy to use is an important output from this.

#### *Typography*

Typography can be defined as designing with type in order to communicate a message. The typeface used and other elements of graphic design such as colour of text need to be chosen with the audience in mind. When used well these aspects organise and communicate the information in a way which meets the needs of the reader. No matter how well written the text is in the PIL, if it is set out in a typography which is difficult to read it is unlikely that patients will take the time or be encouraged to read it.

White space within the written text is helpful in creating a feeling of openness about the information being presented. The use of columns, which are familiar to most readers through newsprint, help readers to easily assimilate information. Line length and line spacing are important aspects of design and should be taken into account when deciding on an appropriate layout.

### *Clear language*

This is already a legal requirement for PILs. Regulation 260 of the HMRs requires that the information is legible, clear and easy to use. If the PIL looks attractive but still retains the use of poor English, or the widespread use of technical terminology again the opportunity to communicate with the patient will be lost.

## **6.2 The intended audience and how this will help meet their needs**

Before writing the information and setting it out on the page you will need to consider where the medicine is going to be used, who will be taking it and what particular issues will need to be resolved. Involving potential patients at an early stage in the drafting of the PIL should ensure success in the testing later on.

There is scope to consider the needs of older people, those whose first language may not be English, people with learning difficulties or those with a condition (for example diabetes) which may affect their vision. Key patient groups which should be considered are set out below.

### Children or young adults

If the medicine is used by these patients you will need to consider how the information needs of this special population are being met by the document. You might need to signpost the reader to other sources of information specifically tailored to that age group or provide a tear-off section of the leaflet which covers the key messages for safe use in a way that they can easily access the information provided.

### Hospital products

If the medicine is being administered or used in hospital or in a clinic setting you will need to consider how the information for the clinical staff and the patient can be separated at the point of use so that each has access to information which is relevant to them.

Information for the healthcare professional will need to be presented in a separate tear-off portion of the leaflet which addresses the issues they need to be aware of whilst administering the medicine.

The patient needs access to the statutory information which provides them with key messages for safe use and which they can retain.

## Eye preparations

If the medicine is an eye-preparation you will need to make sure that the text size for the information is sufficiently large to enable patients who may have sight difficulties to easily read the information provided. This may mean you need to consider the use of a larger document, or that you need to consider alternative designs (landscape rather than portrait for example) to maximise the space available.

### **6.3 Key information for the patient**

Before writing the information and setting it out on the page you will need to decide for each medicine what the key messages for safe use are for the product. This will enable you to consider what information to include in headlines and which particular pieces of information need to stand out to the reader.

Having defined the key messages for safe use with each medicine you will then be able to use these to devise a questionnaire for any user testing which is required to demonstrate compliance with Regulation 260(3) of the HMRs which requires target groups to be consulted.

### **6.4 Helping patients navigate the information**

How the information is set out in the document is important. The order in which the information must be presented is prescribed in the legislation.

You will then need to think about how you place headings and sub-headings on the page to help the reader navigate the information. Headings within the PIL are a vital means of seeing at glance how the information works.

Headings serve two functions:

- they indicate where a section starts and help the reader to *find* the information they are looking for.
- a heading tells you what sort of information will appear in the section below so helping the reader to understand the information.

Headings must be visually prominent so that readers can easily distinguish a heading from the rest of the document. This makes scanning the document for particular pieces of information easier.

Prominence can be achieved in a number of ways and may include:

- the use of reversed text – white lettering on a dark background
- heading text larger than the information which follows and in a bold font
- heading text larger than the information which follows in a strong contrasting colour

Headings must accurately describe the contents of the section of text which follows. The heading should be shorter than the information which follows.

Some sections within the leaflet are lengthy and benefit from the use of sub-headings to further aid the reader find their way through the information which follows. This is particularly important for section 2 of the PIL which will require the careful use of headings and sub-headings in a suitable hierarchy to partition the different pieces of information which must appear here.

## **6.5 Other factors to consider**

Other items which are useful to consider in improving the design and layout of the information include factors such as the use of colour, symbols and pictograms to aid understanding and location of key pieces of information. Additional information is available in annex 6 of ARTL.

In 2007 the MHRA undertook a survey of contractors who regularly carry out user testing for MAHs. A number of key points came out from this in relation to design and layout:

- Make sure headings are placed consistently and stand out by using either a larger font or by emboldening the text
- Judicious use of colour can help but make sure contrast is good and there are not too many colours which can in itself be a problem
- Patients like an index. This is very important if you are using a booklet format which is known to be more difficult to navigate
- Make sure the text size used is as large as possible and that there is good use of white space. Dense text means patients lose concentration and therefore cannot find the information required
- Long lists of side effects are frightening and short bullet points have been found to be helpful. Group the side effects by seriousness and make sure that where patients need to take urgent action this is clear
- Make sure related information is located together and not split over different columns or sides of the leaflet

Additionally, the MHRA has published a set of Quality Criteria which are attached in annex 1. When applied to a leaflet intended for submission, these quickly provide a numerical score which gives an indication of quality and where further changes could increase the score allocated.

## **7. Compliance with Regulation 260(3) of the HMRs – User testing**

### **7.1 Legal Basis**

The legal basis for user testing is set out in Regulation 260(3) of the HMRs.



This states: A package leaflet relating to a medicinal product must be legible, clear and easy to use, and the applicant for, or holder of, a marketing authorisation ... .. must ensure that target patient groups are consulted in order to achieve this.

User testing or other form of patient consultation ensures that patients' views on the content and design and layout are taken into account so that the final leaflet which is submitted as part of the MA enables most medicine users to take safe and accurate decisions about their medicines

## **7.2 What user testing is**

ARTL describes one method of testing the leaflet but recognises that other methods may be valid provided they demonstrate the patients using the document can both find and understand key messages for safe use associated with the particular medicine.

The method described is a diagnostic test which shows how the leaflet performs in practice rather than a content-based test such as a Simple Measure of Gobbledygook (SMOG) test. Diagnostic user testing of patient information leaflets was pioneered in Australia in the early 1990s, and was recommended in guidelines on Readability in Europe by the European Commission in 1999. It is a performance-based, flexible development tool which identifies barriers to people's ability to understand and use the information presented and indicates problem areas which should be rectified. It is particularly useful as part of a leaflet development process. If testing reveals barriers to understanding, carefully considered changes to the leaflet will be needed to improve it.

Some user test companies have employed other methods which are acceptable to the regulatory agencies. Those who have, recognise the importance of observing one-to-one interviews to help understand how patients navigate the information provided.

Key points are set out below.

MHRA will not require any particular method of testing to have been used, but will look for evidence that people who are likely to rely on the leaflet can find and appropriately use the information.

As the MA holder, you are advised to ensure that you have:

- clearly defined before the test what the most important information is – for example, what the medicine is for, the dosage and any significant side effects and warnings. This will vary depending on the active substance in the medicine in question. The questions asked of the participants should cover the key messages for safe use. These key messages for safe use are most likely to come from sections 1 – 4 of the leaflet but the

distribution and spread of questions will vary from one medicine to another. Although for some medicines there may be a need to ask a question from sections 5 or 6 this would not be usual. Make sure you cover all the key messages for safe use in the questionnaire to be sure of a successful outcome.

- reflected in the test sample populations who are particularly likely to rely on the leaflet for the medicine in question (these may include carers). It will not be essential to reflect all patient populations in every circumstance – it will be sufficient that those involved can imagine having the condition for which the product is indicated. Healthcare professionals and other staff and people who routinely work with medicines information must be excluded to avoid bias. People who are familiar with the medicine would not normally be appropriate, although they can be a useful source of advice in the design stage.
- provided credible evidence that test participants can find and appropriately use the information. The questions included in the protocol will be assessed to ensure that they reflect the key safety messages identified. Questions must be open and allow the participant to imagine themselves in a particular scenario, and must not lead them to the answer within the PIL. Each question must perform satisfactorily. It is not appropriate for data to be accumulated and for one or more key messages not to be found and understood by participants. Assessors will be looking for relevant questions to be asked of participants and for each question to individually meet the success criteria determined prior to testing.

#### **Interpretation of the Success Criteria**

- Success criteria were published in “*Always Read the Leaflet*”. These state that 90% of literate adults should be able to find the information and of these 90% should be able to understand the information. Over two rounds of 10 participants on the final proposed leaflet we would expect 16/20 participants to have both found and understood the information. Where results fall below this level we would expect revisions to the PIL to be made and further testing to be carried out. Where alternative test methods are proposed different success criteria may be appropriate. Whatever success criteria are proposed, each question must satisfy the criteria individually.

#### **Preparing the report for submission**

In putting together the report for submission to the regulatory agencies you should take into account guidance already published and available from the [Heads of Agencies](#) website. It is helpful to include the following sections in the report:

Key messages for safe use.

- Identify these up-front for the particular medicine
- Discuss how the questions have been derived based on the key messages for safe use

#### Participant selection and demographics

- Discuss how the participant population chosen reflects the likely patient population for the medicine in question, both in sex and age spread.
- Discuss exclusion criteria and educational level of participants to ensure bias is removed.

#### Report each round of testing

- Graphical representation works well but if graphs are used they must be clearly labelled and easy to interpret.
- Each question must pass the success criteria.
- Indicate which questions participants have problems with. This may be in terms of location or understanding or both.
- If you use subjective criteria such as “easily”, “with difficulty” etc to describe how participants find information, please be aware that we would consider those responses stating “with difficulty” or “with lots of difficulty” to be unsuccessful and that you should discuss how ease of finding the information can be improved by making changes to the PIL.
- Propose changes to the PIL to address the difficulties
- Retest and report further rounds

Discuss any general feedback from the participants on the leaflet and propose changes to address any concerns of a general nature.

- Include all versions of the leaflet.
- We do not need the original data obtained from the interviews – a summary of the verbatim responses will suffice. If we feel we need more information we will ask you for it during the assessment.
- You should not submit data on how each participant performed during the test. The leaflet is being tested, not the participants, and therefore these data are not relevant.

### **7.3 When user testing is required**

All MAs must provide evidence that the provisions of Regulation 260(3) of the HMRs have been met. An applicant is not exempted from these provisions because the medicine in question is a generic version of a previously marketed product. However, this does not mean that a user test (or similar) will have been carried out on all PILs.

When carrying out a user test or other test to demonstrate compliance, a full colour mock-up of the leaflet intended for marketing must be used. It is not acceptable to use a “text” version since design and layout have a significant influence on a patient’s ability to find and understand key messages for safe use.

Leaflets for medicines administered by healthcare professionals in a hospital or clinic setting must still have supporting data demonstrating that they comply with the provisions.

A user test (or similar) will always be required for PILs in the following circumstances:

- medicines which include new chemical entities
- those medicines which have undergone a change in legal status
- medicines with a novel presentation
- where there are particularly critical safety issues
- when significant changes are introduced to the design and layout of a previously tested PIL. Often it is necessary to alter the dimensions of a leaflet to suit a new production facility. Where the orientation and placement of the information remains the same this will not necessitate the need for further testing or a bridging study to be carried out. Changes in orientation and/or placement of text size of text and introduction of alternative formats (flat leaflet moving to booklet) on the other hand will require supplementary bridging data, focus testing or in some cases a full user test to be carried out.
- where a label serves to communicate the information required by Schedule 27 of the HMRs this will need to be subject to user testing.
- where significant new safety information has been introduced into a previously tested PIL. This is likely to include all or some of the following:
  - addition of large amounts of new clinical advice (more than single words or phrases) due to safety restrictions
  - exposure to new patient populations as a result of extending the use of the product
  - major safety reviews

These changes can result in the movement of blocks of text, a reduction in font size, re-orientation of the information, change in design and layout often with the introduction of additional columns or the use of a booklet. All of these design changes will not have been considered in any previous user test or bridging study carried out and will need further data demonstrating compliance with Regulation 260(3) of the HMRs.

Applicants are advised to consult the Product Information Quality Unit for specific advice on particular cases: [patient.information@mhra.gsi.gov.uk](mailto:patient.information@mhra.gsi.gov.uk)

A user test (or similar) will not be required when changes to the leaflet are to introduce a new word or phrase within a section which has previously been subject to testing or when the changes to the design and layout do not impact on placement or size of the information presented.

## **7.4 Submission of a bridging study**

The term bridging has been described to apply to leaflets which are sufficiently similar in both content and layout. In bridging, a successful user test on one PIL (the “parent” PIL) can be used as a justification for not testing other similar leaflets (“daughter” PILs). In some circumstances it may be appropriate for some “daughter PILs to rely on the results of testing for more than one “parent” PIL.

Since the design and layout of the information is crucial to how the information is used and understood, “daughter” PILs should be of the same design, layout and writing style as the “parent” PIL in order for bridging to be successful. A bridging proposal is unlikely to be acceptable to the regulatory body where this concept has not been adhered to.

### **7.4.1 Key messages for safe use**

A successful user test will have identified the key messages for safe use with the particular medicine in question. For each medicine these messages will be different. The questionnaire will have to address these key messages and provide evidence that patients can find and understand these messages so that they can use the medicine safely. Such a user test could then be relied upon to support a PIL drawn up in the same manner for a closely related medicine. In a bridging study the key messages for safe use for both the “parent” and “daughter” PILs need not be identical. However, high profile safety issues should be included in the key points tested for each daughter PIL.

### **7.4.2 Format, design and layout**

The design and layout of the information in the PIL is crucial to the way in which patients access the key messages for safe use. Most marketing authorisation holders have a recognisable “house style” in this regard. In order for bridging to be successful both the “parent” and “daughter” PILs should have a common design and layout. Common design and layout will include the following important aspects:

- font style and font size
- headings and sub-headings including consistency of placement
- PIL dimensions including whether the document is laid out in portrait or landscape format and number of columns
- use of colour and choice of colour
- style of writing and language used
- layout of critical safety sections of the PIL
- use of pictograms

Each different leaflet design (with particular dimensions) or variations in format (such as a booklet, or peelable leaflet) will need to have been the subject of a number of successful user test exercises in order for other leaflets to claim similarity to a particular format in a bridging study. The number of tests required

for a particular format will depend on the complexity of the information conveyed in each case and will be judged on a case-by-case basis.

### **7.4.3 Applying bridging in practice**

There may be particular circumstances where bridging could be used. In all cases the target patient population will be similar.

#### **(a) Line Extensions**

Bridging will normally be acceptable for PILs of the same active **substance** for different strengths or routes of administration. In these cases the “parent” PIL should be the one which contains the more/most complex information for the patient.

For example the PIL for diazepam oral solution could be designated the “parent” PIL for diazepam tablets (“daughter” PIL).

Where a medicine is presented in a formulation not normally supplied to patients for self-medication the relevant PIL could be bridged to that for the same medicine which is self-administered.

For example the PIL for diazepam injection (“daughter”) could be bridged to the PIL for diazepam oral solution (“parent”).

Where potentially similar products require the patient to understand significantly different methods of administration different criteria will apply. Examples include but are not restricted to an inhalation device and a patch. Here it will be important to ensure that the information in relation to the posology has been the subject of a successful user test. However, a “daughter” PIL could rely on user tests carried out on the PILs associated with more than one product.

For example a “double” bridge could be applied to the PIL for a salbutamol inhaler (“daughter”) which could be bridged to a successful user test for a PIL for an oral salbutamol preparation (covers information relating to the active moiety) and to the PIL for a beclometasone product with an identical inhaler device (covers information relating to delivery).

Where a company portfolio includes a range of conventional topical dosage forms (ointments; creams; eye, ear or nose drops or ointments/creams; scalp applications; lotions), individual tests of the administration instructions will not normally be required unless these contain untested pictograms (see below).

However, the requirement remains that the daughter PILs must be of the same design, layout and writing style.

**(b) Medicines in the same “drug class”**

Bridging will normally be acceptable for PILs for medicines in the same therapeutic class where the clinical information set out in the summary of product characteristics (and therefore the information in the PIL) is similar. Importantly the key messages for safe use with the related medicines should be similar. The format and layout of the PILs to be bridged should be identical. This means that the “daughter” PIL should be revised and drawn up in a design, layout and linguistic style which conform to the “parent” PIL which will have been the subject of a successful user test.

A therapeutically similar product is defined as a group of medicines which have similar modes of action. The following examples are included but this list is not exhaustive and inclusion of these therapeutically similar examples within particular classes does not necessarily mean that bridging will automatically be accepted by the MHRA for PILs in these categories:

Cardio-vascular:

- thiazide and related diuretics,
- beta-blockers,
- ace-inhibitors

CNS:

- SSRIs
- tricyclic and similar anti-depressants
- anti-histamines
- benzodiazepines
- opioid analgesics

Anti-infectives:

- penicillins, cephalosporins & macrolides
- antifungals

Musculo-skeletal:

- NSAIDs

Endocrine:

- Glucocorticoids

Malignant Disease:

- alkylating cytotoxics

Nutrition:

- intravenous nutrition

Obstetrics/Gynaenaecology:

- oral contraceptives

Medicines which are considered to be a “group” simply in terms of the therapy area they cover but which actually contain many different medicines with differing modes of action and key messages for safe use will be considered on a case by case basis.

For example the following medicines will not normally be considered appropriate for successful bridging due to the differing clinical considerations:

- Anti-arrythmics such as amiodarone and disopyramide
- Anti-epileptics such as valproate, lamotrigine and phenytoin
- Disease modifying anti-rheumatics such as gold and penicillamine

In therapy areas where there are many different medicines with differing modes of action but the key issues around safe use are much less critical, bridging may be acceptable. The following are given as examples

- Antacids and anti-spasmodics
- cough preparations
- vitamins
- mouthwashes
- emollients and skin cleansers.

In most cases, the chosen parent PIL will be that containing the widest range of information.

### **(c) Same key messages for safe use**

Where the key messages for safe use which have been identified for a range of medicines are similar and the PILs are designed, laid out and written in an identical manner bridging here will be easiest to justify.

### **(d) Same patient population**

Medicines within the same therapeutic class are normally used within the same patient population. However, a small number of medicines are used in more than one therapeutic area. An example of this would be glucocorticoids. In such examples “double” bridging can be applied making sure that the “parent” PILs to which the “daughter” PILs are bridged covers all key messages for safe use arising from the contraindications, warnings precautions and side effects and also addresses issues relating to indications and posology.

### **(e) Combination medicines**



Generally, the PIL for the combination medicine should be considered as the “parent” PIL for the purpose of bridging to the individual component “daughter” PILs. You will need to make sure that any key messages for safe use relating to the individual components have been addressed in the questionnaire for the combination PIL. It may be possible to use the individual component PILs as the “parent” PILs and bridge to the combination PIL as the “daughter” provided any differences in layout and length of the combination PIL have been the subject of successful user testing within the company portfolio.

**(f) Short PILs for medicines with minor therapeutic actions**

Short PILs for such products are unlikely to need to be the subject of a specific user test. It will be sufficient to rely on the successful tests carried out for other products within the portfolio even though these may not be in the same therapeutic class. Examples of such medicines are water for injection, aqueous cream, hypromellose eye drops.

**(g) OTC medicines with a variety of minor components**

Remedies and OTC products with multiple ingredients can be bridged with PILs which have been successfully tested for the main active ingredient(s) e.g. compound analgesics based on paracetamol. The requirements for the PIL format to be the same still apply.

**(h) Pictograms**

Pictograms used within a company house style will need to be tested as part of a user test. For bridging to encompass pictograms successfully the pictograms in “daughter” PILs should have the same design, dimensions and colours as those in the “parent” PIL.

**(i) Bridging between companies**

Each company is expected to rely on his own data. However, if a letter of access is provided, a second company may apply to use the same PIL as another marketing authorisation holder provided the content of the PIL (with the exception of specific company information) is identical. In both cases the design and layout for the PILs concerned should be identical in all aspects as discussed above. The use of different company logos will be acceptable provided these are placed consistently in the two PILs and take up a similar amount of space. A statement should also be made that the applicant has seen the originator’s data and confirm that the user test was acceptable.

**7.4.4 Drafting and submitting a bridging report**

Each marketing authorisation will have to include data which demonstrates that patients can find and understand the information which is necessary for safe and effective use. A bridging report is a full report – but will not include the original data submitted in respect of the “parent” PIL. The user test for the “parent” PIL

should have been submitted and approved prior to the approval of the “daughter” PIL(s). That does not prevent a series of PILs being submitted at the same time for assessment thereby enabling you to take advantage of the bulk fee arrangements.

**(a) Identifying the key messages for safe use**

The bridging report will need to discuss first of all the key messages for safe use within the “daughter” PIL and justify how these are covered within the test carried out on the “parent” PIL. Where the key messages are not identical (and this will apply to many bridged PILs) the bridging report will need to critically appraise these differences and address the relevance of the questionnaire to the “daughter” PIL. Synergies and similarities in the key messages should be discussed.

**(b) Design and layout issues**

There will need to be a critical comparison of the design and layout of both “daughter” and “parent” PILs and synergies and similarities drawn out in support of the bridging exercise.

**(c) Complexity of message and language used**

A critical discussion of the complexity of the messages contained within the “parent” and “daughter” PILs should be presented. The language used in both PILs should be discussed and compared.

All reports should address any general issues raised by participants in the user test concerning aspects of the PIL which they liked or disliked.

## **7.5 Carrying out a focus test**

A focus test may be appropriate in a number of circumstances. A focus test will look at a specific area of the leaflet only and may be used to support a particular change to the leaflet (following a change to the SmPC) or as part of the initial grant of the MA where a discreet aspect of the leaflet cannot be assured by means of bridging to already approved PILs.

A focus test will be carried out in a similar manner to a full user test. However, a smaller set of questions will be needed as only a discreet portion of the PIL is being tested. Participant groupings, however, will need to follow the guidance above for a full user test in order to provide a robust data set for review. The guidance concerning success criteria is also relevant.

Because a focus test is likely to take a shorter time than a full user test you may carry this out using participants drawn together for a full user test on a PIL for a different product during the same user testing session.

## **7.6 Assessment of the data submitted in line with Regulation 260(3) of the HMRs**

First, the MHRA assessor will consider whether the PIL meets the legal requirements as set out in Schedule 27 of the HMRs, including the order of the information.

The assessor will then consider the design and layout of the leaflet, including the font style and size and the way in which the information is written and make a decision on the overall readability of the PIL as intended for marketing.

We will then consider which key pieces of safety information are essential for safe use of the medicine and judge whether or not the applicant has identified a similar set of key safety messages for inclusion within the protocol and questionnaire for the user test.

The user test (or other form of consultation with target patient groups) will then be assessed. The assessor will be looking for evidence that the participants in the test have been able to first find and then understand those key safety messages identified prior to undertaking the testing. The suitability of subjects will be considered by the assessor and you will need to make sure sufficient detail is provided in the report concerning their background and their relevance to the target patient population for the medicine in question. Participants should not be used more frequently than once every six months to take part in such testing. The MHRA will be flexible in the application of the success criteria. However, where the data indicate that patients experience difficulties with particular questions, revisions to the way in which the information is expressed may be required.

## **8. Inclusion of non-statutory information in line with Regulation 261 of the HMRs**

### **8.1 Legal basis**

Regulation 261 of the HMRs permits the inclusion on the label and in the patient information leaflet (PIL) of other information compatible with the Summary of Product Characteristics (SmPC), which is useful for the patient and, importantly, not promotional.

Many patients, particularly those who take prescription medicines long-term, will benefit from additional information about the way in which the medicine works and the disease it is intended to treat.

Information permitted under this category may include additional facts about the use of the medicine and also general background information about the disease and how to manage it. Further advice on how to include information about the benefits of using the product in the PIL itself is provided in Section 3 of the Risk Communication guidance in [Always read the leaflet](#).

## **8.2 Signposting to other sources of information**

The Patient Information Leaflet (PIL) has a key part to play in providing information to patients about their medicine, to promote safe use of the product.

The primary focus of companies should be on ensuring that the PIL provides good information on the use of the product but one PIL cannot meet all the information needs of all patients. We recognise that additional information may be sought by some medicine takers. This guidance sets out additional measures that can be taken to use the PIL as a signpost to sources of further information for patients.

Examples may include details of patient support organisations or services provided by the manufacturer such as leaflets, magazines and telephone support. All materials should be designed to support patients in making informed choices about their healthcare.

The three key principles in the legislation must also be applied to materials accessed via the PIL:

- the information must be compatible with the SmPC. This means the information must relate to the approved indications and usage of the product
- it must be useful to patients and/or carers for the purpose of health education, as described above
- all materials must be non-promotional – information about therapeutic options must not be included in the PIL itself. A balanced overview of the therapeutic options and their place in recognised therapeutic regimes can be provided in supporting materials but comparative statements (e.g. newer/ more effective/ better tolerated/ more evidence to support use than another medicine, etc.) are not permitted.

## **8.3 What can be signposted**

This will depend on the medicine. The company should consider the target populations which are likely to use the medicine and the types of information that patients may find useful. It may be helpful to take advice from a patient support organisation or patient reference group.

Signposts may be to general sources of information relevant to most, if not all medicines or to specific sources that relate to the specific condition and medicine.

Where an external source of information is cited in a PIL, it is important that procedures are in place to perform regular checks to ensure that the information remains current. Address changes for agreed signposts can be made to the MHRA via a notification.

Suggested generic wordings are included for some of the requests but it is up to the company to ensure that the specific wording chosen is accessible and comprehensible to readers with a wide range of reading skills.

## **8.4 Possible signposts**

### **8.4.1 Signposting to patient organisations**

Patient organisations are a valuable source of further information and support for patients and can provide patient-centred information about specific diseases and their management and treatment. They often run helplines and have a range of paper and website based information resources to support patients.

It is permissible to include details of an independent patient organisation including postal, telephone, helpline and website addresses in the PIL.

### **8.4.2 Signposting to general sources of medical information**

There are a number of reputable general sources of information and advice available such as general patient organisations, the [NHS Direct](#) online and [NHS Choices](#) websites or the [PAGB Consumer Health Information Centre](#).

Suggested wordings could include “For further information, go to ...” or “To find out more about ..., go to ...”.

### **8.4.3 Signposting to patient Yellow Card reporting**

It can be helpful to signpost to the availability of patient reporting for suspected adverse drug reactions. This is likely to be most useful for new medicines that are undergoing intensive monitoring and where there is a specific need to collect data on an area of concern, for example in patient populations identified in a Risk Management Plan.

Details of the proposed wording are as follows:

“You can help to make sure that medicines remain as safe as possible by reporting any unwanted side effects via the internet at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). Alternatively, you can call Freephone 0808 100 3352 (available from 10 a.m. to 2 p.m. Mondays to Fridays) or fill in a paper form available from your local pharmacy.”

### **8.4.4 Signposting to information in alternative formats**

The PIL is the most obvious way for companies to make people aware of the availability of alternative formats of the leaflet such as Braille, CD, audio or large print for example. Place this prominently in the leaflet in at least 14 point bold text.

Possible wordings include:

"Is this leaflet hard to see or read? Phone 0123 456789 for help"

"Reading or sight problems? Call 0123 456789 for help"

"For information in large print, tape, CD or Braille, phone 0123 456789"

"Call 0123 456789 for a leaflet in large print, tape, CD or Braille"

"Hard to read? Call 0123 456789 for help"

### **Different formats for blind and partially sighted people**

Many people who cannot read the PIL could access the information if the PIL were provided in another format. The legal provisions require MA holders to provide the statutory information in a format suitable for blind and partially sighted medicine users. This can be achieved in a number of ways and what is provided will depend on user preference. You should ensure that you are able to provide the statutory information in any format which may be requested on behalf of the user.

Large print versions of the leaflet would help many people with sight loss. They may also be easier to read for some people with learning difficulties. Individuals have different preferences, so it is probably more useful to have the facility to print in a range of font sizes than to choose a single option. The usual range of font sizes is 16-24 using a clear font which is either roman, semi-bold or bold.

Audiotape or CD versions of the leaflet can help people with sight loss, those with limited command of English who can understand the spoken word better than written text, and people with reading or learning difficulties.

Braille versions can be useful for the approximately 20,000 Braille readers in the UK. Separate [guidance on the provision of leaflets in Braille](#) is available from the European Commission, and the UK will develop its own supplementary guidance to help MA holders meet this obligation nationally.

Electronic versions of the leaflet include email and Microsoft Word documents which can be sent on a CD-ROM, attached to an email or downloaded from a website. These can be useful for blind or partially sighted people, people who use a computer with text-to-speech or screen magnification software, or other 'access technology' devices. Website standards are available to ensure that the format of the material is suitable for use with the access technologies referred to above.

### **Fulfilling orders for alternative formats**

The helpline number may be that of a company Medical Information Department or a third party contractor under a service agreement. Make sure that there is appropriate quality assurance checking so that the current PIL is provided.

The PIL supplied in alternative format must be identical to the currently approved PIL. To avoid confusion, companies may need to have in place measures to explain why there may appear to be differences if a PIL has recently been updated.

Medicine users' individual requirements and preferences differ, so you may find it easier to have the resources available to prepare PILs in alternative formats on

demand rather than holding a store in several different formats which would become obsolete whenever any change is made to the PIL.

You must not use any information about consumers gained by this means for other purposes.

#### **8.4.5 Signposting to additional company materials**

Before designing an additional leaflet, website or audiovisual material, companies should identify whether the desired outcome can be achieved by simplifying the existing PIL without loss of information or by providing additional information in the PIL that would be of use to patients and carers. Companies should also consider the benefits of working with a patient organisation to ensure that the proposed materials meet the needs of patients. Materials must always be non-promotional. Care should also be taken to ensure that any information on the condition and its treatment is consistent with current clinical practice and any available national guidance, for example from the National Institute of Care Excellence (NICE) or the Scottish Medicines Consortium.

In the past, companies have often also provided additional patient support materials to prescribers to pass on to their patients. This relies on memory and availability of materials at the time of consultation. Information in the PIL provides an alternative source that could help to overcome this.

Additional leaflets such as a leaflet for carers or for children prescribed a medicine cannot always be provided in the pack due to packaging constraints, but a reference to their availability could be placed in the PIL. Such materials must always be non-promotional.

Simplified leaflets may help people with literacy or learning difficulties or a limited command of English. They may also help older children to understand how to use their medicine.

Videos are likely to be of most use in helping to explain complex instructions such as how to take an inhaled medicine or prepare a complex product.

Booklets can provide additional information, such as disease awareness material or information targeted at particular groups, but consideration should always be given to whether the information could be included in the PIL as that is more likely to reach the user.

Magazines can help to support people who use a medicine long-term. There must always be a clear procedure to unsubscribe for repeat materials.

Helplines, which may take the form of recorded information or a live advice service, can also help most people with special access needs. Where a helpline is publicised in a PIL, a copy of the script or the recorded information should be

provided to the MHRA Product Information Unit in advance to ensure that the content complies with the legal requirements.

A leaflet in another language may benefit people with limited command of English. This option is especially relevant where a disease is particularly prevalent in certain ethnic populations. A faithful translation of the English version must be obtained. This need not be verbatim but must adequately convey the intended messages. When commissioning translations you should verify the quality standards of translation services.

#### **8.4.6 Signposting to company-sponsored websites**

Websites containing materials to support use of the product may be permitted as part of the extra-statutory information in the PIL and inclusion of the website address will be considered on a case-by-case basis. Products which are for long term conditions or where additional support is required during treatment are most suitable for this type of signposting. In all cases details of the website content must be submitted to the MHRA for assessment and importantly must not be promotional in line with the provisions of Regulation 261 of the HMRs.

#### **8.5 Quality assurance of additional sources of information**

It is good practice to ensure that additional materials achieve their aim.

Options to achieve this include:

##### **8.5.1 MHRA review**

The MHRA currently asks to review all materials signposted from the PIL when the signpost is first agreed.



## 8.5.2 Accreditation

The Information Standard scheme (<http://www.theinformationstandard.org>) was developed by the Department of Health and Social Care to help the public identify trustworthy health and social care information easily. The standard itself comprises a set of criteria that defines good quality health or social care information and the methods needed to produce it. To achieve the standard, organisations have to show that their processes and systems produce information that is accurate, impartial, balanced, evidence-based, accessible and well-written.

The assessment of information producers is provided by independent certification bodies accredited by The United Kingdom Accreditation Service (UKAS). Organisations that meet the standard can place the quality mark on their information materials and their website - a reliable symbol of quality and assurance.

## 8.5.3 Compliance with Codes of Practice

### Prescription medicines

The ABPI Code of Practice for the pharmaceutical industry covers all materials developed for patient support by companies marketing prescription medicines. The Code is administered by the Prescription Medicines Code of Practice Authority (PMCPA) which acts independently from ABPI to investigate complaints from health professionals, competitors or the public. The main sanction is withdrawal of the material and publication of a report but there are also a range of other options including issue of a correction, recall of materials, audit of procedures by the PMCPA and suspension from ABPI membership.

The Code of Practice also sets standards for interactions between companies and patient organisations. It requires companies working with patient organisations to have a written agreement setting out the purpose and extent of the collaborations. This should cover development of materials and matters such as use of the organisation's logo. Companies are also required to report annually on the support given to patient organisations.

Copies of the current Code and details of the work of the [PMCPA](#) are available on their website.

### Over the counter medicines

The PAGB Consumer Medicines Advertising Code covers materials developed for consumers by companies that relate to medicines available for purchase. PAGB vets all materials aimed at the public

prior to issue to ensure compliance with the Code. Any complaints about materials would be investigated by the [MHRA Advertising Standards Unit](#).

## **8.6. Further resources**

### **8.6.1 Website standards**

[RNIB Web Access Centre](#) provides useful advice on testing the accessibility of website information and links to other services. Health on the Net ([HON](#)) [Foundation](#) provides advice and accreditation of website material under the HONCode.

British Standard BS 8878:2010 outlines a framework for web accessibility, to meet the requirements of the Equality Act 2010. The code of practice is designed to help ensure that all products delivered via a web browser can be accessed by anyone.

### **8.6.2 Other sources of advice and support on writing health information**

#### **NICE guidance**

NICE (the National Institute for Health and Clinical Excellence) issued clinical guidance on “Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence” in January 2009. [This guidance](#) is about enabling patients to make informed choices by involving and supporting them in decisions about prescribed medicines, including the role of information provision.

#### **DH/ODI guidance**

The Department of Health and Office for Disability Issues published [good practice guidance aimed at people who commission easy read information for people with learning disabilities, as well as further advice](#). This guidance is mainly for public sector organisations at a local and national level, but also for other organisations which produce public information specifically for people with learning disabilities.

#### **Plain English campaign**

[The Plain English campaign](#) offers advice and guidelines and can apply their quality ‘Crystal Mark’.

#### **Communication Research Institute of Australia**

‘Writing about medicines for people’ by D Sless & R Wiseman, is available from [the Communication Research Institute of Australia](#). It draws on Australian experience of writing consumer medicines information. The website also lists other relevant Australian guidance.

## **9. Conclusion**

All applications submitted (either via the application process or via the notification scheme) to the Medicines and Healthcare products Regulatory Agency that include a patient information component will be considered against the criteria in this document. This will apply in all areas of MHRA work (new MAs, PLPIs, renewals, variations and notifications and applications to the Product Information Quality Unit).

Where a marketing authorisation holder deviates from this guidance a full justification for this should be provided with the application.

Once new packaging components have been accepted or approved by the MHRA these must be introduced into packed stock being certified for release to the market by the Qualified Person within three to six months, unless MAHs have been advised of the need for earlier introduction of the new components for safety reasons. The Qualified Person should not certify a medicinal product for release to the market if the packaging components, at the time of certification, have not been updated within three to six months following approval.

## ANNEX 1

# Quality criteria for PILs

### Process indicators

Evidence of involvement of patients in development

- Score 1 for evidence available; 0 for none

Evidence that needs of special populations have been catered for

- Score 1 for discussion of special groups; 0 for none

User testing carried out/bridged

- Score 1 for yes; 0 for no

### Leaflet indicators

#### a. Scores for presentation - text readability and ease of navigation

All scored on a scale of 0 for examples of poor practice, 1 for acceptable, with up to 3 bonus points for examples of best practice on any criteria (max. 1/criterion)

- Font choice, size and style
  - score 0 for difficult to read; 1 for clear and legible
- Use of text in capitals, italics, underlined, in boxes, etc.
  - score 0 for any example of poor use of these; 1 where these are not used
- Contrast between text and background, colour
  - score 0 for poor colour contrast; 1 where good contrast used
- Format and line spacing
  - score 0 for dense text; 1 for good use of white space
- Use of columns, justification and length of lines, sentences and paragraphs
  - score 0 any example of poor use otherwise score 1;
- Use of headers
  - score 0 for only the main headings as in the QRD template;
  - score 1 where subheadings are used
  - Bonus for use of clear and sensible headings that aid navigation

- Use of symbols and pictures,
  - score 0 where these are used badly without reference to patients; 1 for good use; bonus when these have good evidence to support their use or clear pictorial instructions for use are included

### **b. Scores for content**

All scored on a scale of 0 for poor practice, 1 for acceptable with up to 3 bonus points for examples of best practice on any criteria (max. 1/criterion)

- Pointers to further information sources
  - Score 0 for no signposting; 1 for signposting
- Pointer to availability in alternative formats
  - Score 0 for no signposting; 1 for signposting
- Use of lay terms instead of medical jargon
  - Score 0 where medical jargon persists; 1 for mainly lay terms
- Headline inclusion
  - Score 0 for no headlines; 1 for headlines
- Inclusion of benefit statement
  - Score 0 for no benefit information; 1 for appropriate benefit information
- Grouping of side effects:
  - Score bonus for prominence of key effects with need for action
  - Score 0 where side effects not broken up at all
  - Score 0 where system organ class is used
  - Score 1 where side effects are ordered so that serious side effects come first
- Inclusion and presentation of side effect frequencies:
  - Score 0 where no frequencies or word terms not defined; score 1 where frequencies are stated

Maximum score for leaflet indicators – 20 (10 for presentation + 10 for content)

### **Outcome indicators**

Aim for consistency - informed actions where any medicine usage is in accordance with dosage instructions and actions required to minimise risk.

Surrogate measures:

- ADR reports relating to incorrect usage
- Information from availability and usage surveys including DH Information Prescription work, published surveys (Raynor, etc.)
- Uptake of DH accreditation (when available)
- Complaints from public and health professionals to MHRA about individual PILs
- Company measures: uptake of further information, helpline usage, consumer questions, etc.

- Invited comments from patient organisations, health professionals and public on specific categories as part of planned category review