Improving information for patients: the UK perspective

Introduction
The information given to patients with their medicines has been regulated in the UK since 1977, though few medicines (usually inhaled medicines requiring detailed instructions for use by patients) were supplied with leaflets for patients at that time. In 1992, the European Commission issued Directive 92/27/EEC on the labelling of medicinal products for human use and on package leaflets. The Directive brought together requirements for detailed information that must accompany medicines, to ensure their safe and effective use. It was timed to coincide with the introduction of the new legislation state in which the medicinal product is placed on the market.1

Changes to the legal requirements
Changes to the European legislation made in 20042 introduced a new legal obligation on all marketing authorisation holders to ensure that the PILs reflect the results of consultation with target patient groups (‘user testing’) (Article 59(3)). This was a major step forward in providing regulators with powers to ensure that the PIL is legible, clear and easy to use. A separate amendment to the order of the leaflet information ensured that the important safety messages were now presented in a more logical manner (Article 59(1)).

Implementation in the UK
In 2003, the UK Committee on Safety of Medicines (CSM) set up a Working Group on Patient Information to address the concerns relating to the quality of PILs and to champion improvements to these documents.3-6 The Working Group considered that, as a priority and to coincide with the new legal requirements, greater emphasis on involving patients in the writing of the leaflet, developing guidance in the area of risk communication and meeting patients’ needs, was essential.

The Working Group considered that early implementation of these legal amendments in the UK would provide a significant benefit to public health, enhance patient safety and further the long-term strategy of improving the information provided to patients with their medicines. Consequently, the MHRA undertook a public consultation7 on the proposal to take forward the amendments in the legal provision in advance of the European Commission’s deadline.

A statutory instrument was laid before Parliament in December 2004 to implement the legislative changes in the UK from 1 January 2005.8 All new applications from that date were required to comply with the new legal requirements, with a three-year transitional period for existing products until July 2008. The latter were brought into compliance by either National Article 61(3) notification procedures or by Mutual Recognition Type II medical variation procedures.

Guidance development
Guidance which was available at the time the new provisions came into force was largely focused on specific items of information to be included, and the prescribed order of inclusion. There was relatively little guidance on how best to present information in order to optimise understanding and support the safe use of medicines.9 To assist those having to update their marketing authorisations, the MHRA in conjunction with the CSM Working Group undertook to provide a series of guidance documents.10 The development of these was timed to coincide with the introduction of the new legislation.

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Abstract
For many people, the primary (or only) source of information about their medicine is the patient information leaflet (PIL) which, since 1999, must be provided with all medicines. Patients expect, and are entitled to, good quality information about their medicines, whether prescribed or bought over the counter. Such information is a vital supplement to other forms of communication between healthcare professionals and their patients.

This article looks at the recent legal changes put in place to improve the quality of the statutory patient information in line with new legal requirements in the UK, from the perspective of the Medicines and Healthcare products Regulatory Agency (MHRA).
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Figure 1 and 2 (opposite):
These figures represent the number of Article 61(3) notification submissions received by the MHRA per financial quarter beginning April 2004 to quarter ending June 2009.

**Figure 1** corresponds to actual quarterly data whereas Figure 2 corresponds to the cumulative quarterly data. Prior to July 2005, the average number of Article 61(3) submissions received was 1,500-1,600 per annum.

The data indicate that the number of submissions did not increase significantly from the baseline level until the quarter ending December 2007, which was when the MHRA had expected to have received all leaflet submissions with supporting user test data. In the subsequent six months to the 30 June 2008 deadline, the MHRA received the equivalent of nearly five years’ work compared to baseline. The data also indicate that there is a decreasing trend in number of submissions such that they now appear to be returning to the previous baseline levels, and the number of submissions which have not yet undergone initial assessment is, by comparison, rather small.

**Note**: These data do not include the 1,100 MRP PIL harmonisation variations (with supporting user test data) assessed to date or the other 3,400 BROMI self-certified Article 61(3) notification submissions made to date. The data for July to December 2005 do not accurately reflect the MHRA workload since during this period the submission data were migrated from the former ‘PLUS’ system to its replacement ‘Sentinel’ and a processing backlog developed.

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Case study – Seroxat (paroxetine) PIL

It is known that some patients will not read the patient information leaflet, especially where they perceive it to be too long and/or too complex. In an attempt to ensure that patients are aware of key information on the safe and appropriate use of a product, the guidance encouraged companies to submit proposals for a concise ‘headline’ section at the start of the PIL. This section should focus on information that the patient must be aware of in order to ensure safe and effective use of his/her medicine. Likewise, it is also important that patients understand the potential benefits of their medicine. Such extra-statutory information is supported within the legislation through the provisions of Article 623 provided that it is compatible with the summary of product characteristics (SmPC), useful to the patient and non-promotional.

One way in which the risks of a treatment can be placed in the context of the potential benefits is to include some general information about how the medicine works, the impact that taking the medicine is likely to have on the patient’s wellbeing, to signpost the reader to further information about the disease being treated, lifestyle changes which would also benefit them and details of patient support services.

The PIL plays a vital role in providing clear advice for patients on the risk of side-effects and what actions to take if they encounter problems when taking their medicines. In particular, patients should know whether to continue taking their medicine and when they need to seek medical advice about possible side-effects.

The current Seroxat PIL now includes an opening section entitled ‘Eight important things you need to know about Seroxat’ which includes key information on the benefits of taking the medicine, clear reference to the contraindication in patients under 18 years of age, warnings of suicidal thoughts and behaviour, withdrawal effects and signposting to sources of information (other than the doctor or pharmacist, such as self-help groups or patient organisations) that can provide additional support and advice. In each instance there is a clear reference to the relevant section of the PIL for the fuller information. Within the body of the PIL there is also additional information within section 1: ‘What Seroxat is and what it is used for’, section 3: ‘What to do if you’re feeling no better’, section and also at the end of the PIL regarding the ‘use in children and adolescents under 18 years of age’.

and was the subject of industry consultation. Key issues on which advice and guidance were provided were in relation to improved risk communication and an appropriate method of consulting with target patient groups.

As part of this body of work, the MHRA held a focus group discussion with representatives from patient interest and user groups with respect to the Seroxat (paroxetine) PIL. The aim of this focus group was to obtain views as to whether a revised PIL met the needs of patients taking the medicine. All sections of the PIL were reviewed and areas identified where clarity was required (see Box: Case study – Seroxat (paroxetine) PIL).

While PILs provide comprehensive information that is specific to one medicine, some patients may lack the prior understanding about medicines and side-effects to put this information to best use. With that in mind the Working Group and the MHRA also developed a general leaflet on risks and benefits of medicines called ‘Taking medicines – some questions & answers about side-effects’.11

As time went on and experience with the new requirements was gained, further guidance documents were developed. In addition to working with experts on the CSM Working Group, the MHRA also took into account the views of patients and those who carried out testing on behalf of marketing authorisation holders. The guidance documents will not be discussed in any further detail here, but are all available from the MHRA website.12

Sharing best practice with industry

To promote learning and to share best practice with pharmaceutical companies, the Patient Information Quality (PIQ) unit at the MHRA held three seminars for industry. These seminars included presentations focussing on the new legal requirements, the regulatory objectives and expectations of the regulator, best practice in the design of PILs and methods for carrying out user testing.

Related workshops helped delegates put the learning into practice and gave a more practice-based understanding of the process and how to develop high quality patient information with a likely success of approval on submission. Many companies also made use of the MHRA Scientific Advice provision to discuss the design and layout of their PILs and proposed user testing protocols and schedules.

The MHRA also took the decision to publish a series of examples – ‘PIL of the month’ – to promote and share best practice, to illustrate improvements and to aid learning.12 All leaflets (more than thirty, to date) were published with the agreement of the marketing authorisation holder responsible for the medicine to which they relate.

The PILs in this scheme have been supported by user test data in compliance with Article 59(3). Nevertheless, this is only one aspect of the quality of the information and is not in itself the main endpoint.
Figure 1: Article 61(3) notifications to MHRA April 2004 onwards

Figure 2: Cumulative Article 61(3) notifications to MHRA April 2004 onwards
The quality of the information can be assessed in other ways, and the current Expert Advisory Group on Patient Information has developed a quality scoring system to help identify, by means of a numerical score, good quality patient information.\textsuperscript{12} Marketing authorisation holders may find it helpful to use this scoring system to help develop better quality PILs. Leaflets included in this initiative have scored significantly higher in the new layout and design than they would have previously (eg, the current Seroxat PIL scored 16 compared to 6 in its non-user tested layout).

Managing workload

The MHRA had hoped to avoid a peak of work in the run-up to the deadline – for industry and the agency. Despite a three-year transition period and guidance calling for submissions to be made by the end of December 2007, it became clear by September 2007 that the majority of leaflet submissions (with accompanying user test data) remained to be submitted to the MHRA for approval by 1 July 2008 (see Figures 1 and 2). A best guess at that time was that of the approximately 17,000 granted marketing authorisations in the UK required to comply, 13,000 were yet to comply by the deadline.

Up until that date, the PIQ unit had taken a detailed approach to the assessment, ensuring that the opportunity presented by user testing to improve the quality of PILs had been maximised while still maintaining constant throughput. But it was appreciated that this approach was unsustainable in light of the volume of applications still anticipated, and the timeframe for compliance of all marketing authorisations. The assessment protocol was therefore streamlined to focus on the key information areas of the PIL and removal of the SmPC compliance check. This decision was risk-based on the following:

\begin{itemize}
  \item The leaflets were already in the marketplace and had been assessed as being consistent with the SmPC, and the changes proposed were only in relation to the order of the information and taking patients’ views into account
  \item Very few complaints in relation to patient safety had been received for existing leaflets.
\end{itemize}

This allowed us to re-focus assessors’ workload to specific therapeutic areas, to make best use of experience and to ensure consistency. Early experience allowed us to estimate a ratio of one full assessment to five bridging submissions but even so, with the peak of work still expected, it also became clear that additional resource from assessment areas throughout the agency was also required to handle the influx of submissions. A significant number of marketing authorisation holders still failed to submit applications to update their marketing authorisations by 1 April 2008. Those marketing authorisation holders received a communication from PIQ stating that they must submit either an approvable application,\textsuperscript{11} or a notification that the product would not be marketed, by 30 June 2008 if they failed to submit applications to update their quality, accessibility and potential impact on safe use. The PIL is the only written information that must legally be provided to patients with their medicine, and so affords a unique communication opportunity. Work is ongoing on the development of this guidance, and will be the subject of a consultation later in the year.

3 Promoting consistency. The MHRA also intends to be proactive in engaging with industry to achieve consistency in the information provided to patients. The lack of consistency in the information provided by different manufacturers of the same medicine is one of the most common complaints that the MHRA receives with respect to PILs. Targeting the PILs of the 20 most commonly prescribed products will be fundamental in spreading best practice and in improving the quality of the information for patients.

Conclusion

The majority of marketing authorisations have now demonstrated compliance with the UK legislative requirements for the PIL to reflect consultation with target patient groups (user testing), and this is considered to be a major milestone on the journey to improving the provision of information to patients in the UK. At the end of the process, patients will see the biggest step change in quality information since the requirement for a leaflet was first introduced in the 1990s.

Important as this milestone is, PILs will still not be optimal in terms of their quality, accessibility and potential impact on safe use. The PIL is the only written information that must legally be provided to patients with their medicine, and so affords a unique communication opportunity. Nevertheless, a significant proportion of industry has yet to fully buy-in to the concept of the PIL as a key tool in supporting safe use and good decision-making. Too many PILs are compliant with the requirement to user test and yet are still not fit for purpose. Research\textsuperscript{17} supports that the patient values the leaflet more highly than information from any other source except from a doctor or a pharmacist. Those companies that have embraced the fact that the PIL represents the public face of their medicine have made real strides forward in delivering high quality information that supports its safe use.

The future work of the MHRA, in consultation with its Expert Advisory Group and with the feedback from the patient and public engagement strategy, looks to build on this and improve the quality of patient information still further.
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