Unlicensed medicines use in the UK: A systematic review and quality assessment of published guidelines

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Background

An unlicensed medicine is defined as a medicinal product for which there is no marketing authorisation granted by the Medicines Healthcare and Regulatory Agency (MHRA)[1]. Unlicensed medicines are widely used within the UK and there are many guidance documents which exist to support their use. However, each guidance document is published for individual organisations and there has never been an analysis of the different approaches these documents take nor an evaluation of their quality.

Aims and Objectives

To analyse the content and quality of unlicensed medicines guidance documentation in use in the UK.

Methods

A systematic search of the published literature was conducted between April and June 2015. Databases used to identify published guidance included Medline, Embase, ISI Web of Knowledge, Google Scholar, PubMed and International Pharmaceutical Abstracts. Search terms included 'unlicensed medicine' or 'specials' combined with; guideline, policy, framework, standardized operating procedure, standard operating procedure or recommendation.

Additionally, a call for guidance was also distributed to encourage organisations to submit their guidance documentation for the review. This was distributed to secondary care, primary care, community pharmacy and pharmaceutical industry networks both locally and nationally.

The quality of the guidelines was assessed using the AGREE II tool[2] and content was evaluated by conducting a thematic analysis. The AGREE tool rates the quality of the documentation across six domains and provides a score from 0% for very poor quality to 100% for excellent quality.

Results

A total of 52 guidance documents were included in the analysis. This included those from NHS secondary and tertiary care trusts (n=28), professional bodies and regulators (n=11), community pharmacy organisations (n=3) and others (n=10). Documents included within the analysis ranged from guidelines (n=28), policies (n=10), standard operating procedures (n=9) and frameworks (n=5).

AGREE II scoring revealed that the content of the documents assessed overall scored well in the 'Scope and Purpose' (70.6%) domain and the 'Clarity of Presentation' domain (70.4%). This was due to the documents having specific objectives that were well described within the content of the document and the target audience being easily identifiable. In the majority of cases the presentation of information was good, enabling key recommendations to be easily identified that

were specific and unambiguous. In contrast to these positive results the 'Rigour and Development' domain (12.1%) and the 'Editorial Independence' domain (2.6%) scored poorly. Rigour and development had low scores throughout, due to the lack of documented reference to a clear evidence base. With regards to editorial independence, it was not clear in the majority of cases if there were any funding bodies or competing interests from the guideline development group. In terms of the 'Applicability' domain (23.9%), whilst some documents provided advice and tools in implementation of the recommendations, many did not and there was a deficit in the acknowledgement of the potential barriers and facilitators to implementation of recommendations. The 'Stakeholder development' scores (30%) revealed that it wasn't always apparent if there was a diverse mix of professionals involved in the development of the guidance documentation and there was little to no involvement of the target population in which the guideline was to be used in, in this case patients within the NHS.

Thematic analysis of the guidance documents revealed four parent themes across the documentation which included; responsibility around the use of unlicensed medicines, the practicalities surrounding use of unlicensed medicines, risk versus benefit and controlling use of unlicensed medicines.

Responsibility around the use of unlicensed medicine incorporated subthemes around understanding the definitions around unlicensed medicines which was common to almost all of the guidance documentation analysed, awareness of patients and professionals when using an unlicensed medicine, responsibilities of individuals and organisations involved in using unlicensed medicines and references to the guidance and legislation which informed the individual documents.

The practicalities of using unlicensed medicines included subthemes on selecting the pharmaceutical formulation, the role of the pharmacist and the wider pharmacy team in managing the use of unlicensed medicines, patient involvement, the different stages of using an unlicensed medicine from prescribing to administration, and issues around continuing treatment with unlicensed medicines.

Risk versus benefit in using unlicensed medicines was another strong theme across the guidance documentation. This included discussing the evidence to support use of unlicensed medicines and the place of unlicensed medicines in the treatment of a patient and potential alternatives to their use. Describing and assessing risk associated with unlicensed medicines and emphasising reporting of errors and adverse effects associated with unlicensed medicines was also contained within this theme.

Controlling the use of unlicensed medicines was a theme that described the strategies that various organisations employ in an attempt to address costs associated with unlicensed medicines, audit of unlicensed medicines use against guidance and recommendations, placing restrictions on the use of unlicensed medicines to minimise risk and the use of organisational decision making surrounding unlicensed medicines, such as the use of formulary applications and stratifying risks according to a wide range of criteria.

Discussion

Thematic analysis demonstrated a lack of consistency of content across guidance documentation used for unlicensed medicines.

The AGREE scores exhibit that there is also a lack of transparency around who writes and updates guidance on unlicensed medicines and on what foundations they base their recommendations. The lack of evidence base for the recommendations contained as revealed in the AGREE scores is likely to reflect a wider issue around lack of evidence for unlicensed medicines use. It has also shown that there is a large deficit in patient involvement in guidance development which needs to be addressed.

There was a lack of contribution of documentation from the community pharmacy and primary care sector and it is not clear if this is due to a lack of guidance or a lack of submission to the project for analysis.

Conclusion

Healthcare organisations would benefit from agreeing a ‘core content’ for unlicensed medicines documentation and there is a need for evidence surrounding unlicensed medicines use to be gained and shared to inform decision making around use of unlicensed medicines.

References

1. MHRA. Guidance note 14: The supply of unlicensed medicinal products ("specials"). 2014. http://www.mhra.gov.uk/home/groups/is-lic/documents/publication/con413520.pdf (Accessed 27 August 2015)
2. Brouwers M, Kho ME, Browman GP, Cluzeau F, Feder G, Fervers B, Hanna S, Makarski J. AGREE II: Advancing guideline development, reporting and evaluation in healthcare. Can Med Assoc J. 2010; 182: E839-842