Discussion paper: no 1

Reforms of s12(1) of the Medicines Act 1968: overview

Introduction

1. This informal discussion paper is one of a series prepared by the Medicines and Healthcare products Regulatory Agency (MHRA) which explores possible reforms of section 12(1) of the Medicines Act 1968 and its associated provisions. S12(1) is the legislative provision used by herbal practitioners, and some others, carrying out a business in which they prepare unlicensed herbal medicines to meet the individual needs of patients identified in consultation. The MHRA welcomes dialogue with interested parties on these ideas. The papers are intended to help focus such discussions. This document gives an introduction and overview.

2. The Agency is building on the work of an earlier consultation, issued in 2004. That consultation (MLX 299) and a summary of responses to it are on the MHRA website. The Agency envisages that there will be a further formal public consultation on updated proposals. Work on the s12(1) reforms is being carried forward alongside the related DH-led work programme to develop proposals for the statutory regulation of the herbal medicine profession.

Aims

3. MHRA's aim for herbal medicine is to give consumers continuing access to a wide range of herbal medicines made to assured standards of safety and quality and with appropriate information about the safe use of the product. This can be achieved by three related measures:

   - The traditional herbal registration (THR) scheme, introduced in 2005, under which over the counter (OTC) **manufactured traditional herbal medicines** are required to meet **standards of safety, quality and patient information.** In addition to the THR scheme, the possibility also exists for herbal medicines, like any other, to have a marketing authorisation based on demonstration of safety, quality and efficacy
   - The DH led programme to achieve the **statutory regulation of the herbal medicine profession**. This would give the public safeguards as to the **professional standards and accountability of practitioners**
   - Reform of s12(1) and related provisions to give the public assurance as to the quality and safety **standards of unlicensed herbal medicines made up by or for herbal practitioners.**

Areas covered by the review of Section 12(1)

4. The review covers three main areas:

- s12(1), including improved safeguards for the public; also a possible extension of the scope of the exemption to cover a limited range of non herbal ingredients
- provisions that could permit a registered practitioner to commission a 3rd party to manufacture an unlicensed herbal medicine to meet the special needs of an individual patient
- legislative and other options for restricting or prohibiting use of particular herbal ingredients on safety grounds.

The weaknesses of s12(1)

5. S12 of the Medicines Act 1968 exempts herbal remedies, under certain conditions, from the requirement for a product licence and various other provisions of the Medicines Act[1]. The provisions of s12(1) are used by practitioners to make up and supply unlicensed herbal remedies to meet the needs of individual patients identified in consultation.

6. The main weaknesses of s12(1) are that:

- there are no stipulations that the person carrying out the consultation must have any particular qualifications or experience
- there are no requirements that the person carrying out the consultation should be professionally accountable
- there are no specific requirements as to the quality of the unlicensed herbal medicine supplied; safeguards that apply are more general in nature, eg flowing from general consumer legislation
- there are no specific requirements as to the safety of the unlicensed herbal medicine supplied, other than certain restrictions on named herbal ingredients.

Why is there a need to improve regulation?

7. The case for improved regulation of s12(1) arrangements overlaps to a large extent with the case for improved regulation of OTC manufactured herbal medicines that resulted in the European Directive on traditional herbal medicinal products and the consequent introduction of the traditional herbal registration (THR) scheme for such products. In particular the common theme is the persistent evidence of patchy standards in the manufacture/preparation of unlicensed herbal medicines leading to direct risk to public health. There is, however, a major additional component to the case for reform of s12(1) arrangements, namely that a practitioner is seeking to exercise a judgement about how to meet the health needs of the individual patient and is then preparing a medicine to meet those specific needs. Thus, the competence and professionalism of the practitioner is critical as well as the quality and safety standards of the individual product. It is striking that in response to MLX 299

[1] Section 12 is an exemption from the licensing provisions in the Medicines Act 1968, and is only relevant to medicinal products which in the first place fall outside the scope of Directive 2001/83/EC (eg products which are neither prepared industrially nor prepared using an industrial process).

no respondents argued against the need for reform. Since then further evidence has continued to accumulate. The following are some of the main factors:

Patchy product standards posing risk to public health

- there is continuing evidence of patchy standards in parts of the UK sector; unlicensed remedies on the UK market and supplied by clinics/practitioners have been found variously to contain:
    - potent pharmaceuticals (eg steroids, glibenclamide, fenfluramine, nitrosofenfluramine)
    - very high levels of heavy metals
    - the wrong (and sometimes toxic) herbal ingredient
    - ingredients (such as human placenta or bat excrement) that could transmit infection
- in recent years there has been growth in usage in the UK of herbal medicines from the Ayurvedic tradition and traditional Chinese medicine (TCM) where heavy metals historically have had an accepted place. This poses particular issues for public health
- these incidents are regularly reported on *Herbal Safety News.* It is very probable that significant numbers of cases go undetected given that the current arrangements have limited safeguards
- while some incidents may be small in scale, eg resulting from sourcing low grade products from relatives abroad, others can be more significant. For example, in December 2004 the MHRA confiscated a consignment of 90,000 tablets reportedly containing a toxic ingredient and in 2003 the MHRA found that a product containing 11.7% mercury by weight was available in 35 traditional Chinese medicine outlets. It is probable that this kind of product would have been intended for use in one to one consultations
- the extent of the problem has led the MHRA, its predecessor the MCA, and the former Committee on Safety of Medicines on three occasions in recent years to warn the public about erratic standards of manufacturing in parts of the TCM sector
- there is wide evidence as demonstrated through international exchange of information between regulators, journal articles in a range of different countries, and by the work of the WHO that the issue of a trade in low grade herbal products and ingredients is an international problem
- overall, in no other sector of medicines in the UK would it be regarded as acceptable for there to be such persistent evidence of mismatches between stated and actual ingredients. There is no reason why consumers of herbal medicines should be expected to accept patchy and sometimes low standards simply because the medicine is actually, or reportedly, made from plant material. The MHRA is aware that responsible practitioner organisations are very concerned at the damage to the reputation of the sector from those who engage in irresponsible and/or criminal practice

Actual public health risk from low grade products

- scattered incidents continue to occur in the UK where alert doctors or pharmacists in the health service have identified ill health attributable to unlicensed "herbal" medicines containing undeclared ingredients. Cases have included ones where organ transplant has been required
- in Belgium in 1990s there was a major incident when, following consumption of toxic herbal medicines over 100 women suffered serious kidney damage and some went on to develop cancer. That incident was picked up mainly because of the concentration of women in a particular locality
- in the UK, use of herbal medicines supplied by practitioners and clinics is generally widely diffused across large numbers of small outlets. This means that for a busy clinician in the health service it will typically not be evident (eg as a result of a sudden surge in cases) that a patient's ill health may be due to special factors, of which one of many possible causes could be taking an unlicensed product with an undeclared toxic ingredient. In any case, survey evidence shows that many patients do not tell their doctor that they are taking herbal medicines and/or that doctors don't ask. The illness will thus be treated but no one will know why the patient has a problem such as kidney or liver damage
- in MHRA's view the only prudent assumption should be that in UK in a proportion of cases where ill health is due to low grade, unlicensed herbal products containing a toxic ingredient the causation remains undetected. There are many obstacles to any attempt to estimate the prevalence of ill health caused by this hazard. One of the most fundamental is that it is not possible to test an unlicensed product against the question "what is in this product". It is only possible to test for the presence of particular ingredients. To the best of MHRA's knowledge no one in the UK or in any other comparable country has been able to carry out such a study of the prevalence of ill health caused by low grade products

Increased awareness of area of public health risk with herbal medicines

- scientific knowledge of safety issues relating to adverse drug reactions and to interactions between herbal and conventional medicines continue to develop. Examples include liver damage linked to black cohosh, some herbal medicines affecting the efficacy of anaesthetics, St John's Wort interacting with prescribed medicines. It is reasonably predictable that new areas will continue to emerge. This expanding range of safety issues argues for a requirement that practitioners be professionally competent, accountable and required to keep their knowledge up to date
- many areas of herbal safety have not been well studied such as the use of herbal medicines in pregnancy, while breastfeeding and in children. This similarly argues that practitioners should be professionally competent and in particular should take a precautionary approach to the many areas of uncertainty. This can be best be achieved where practitioners are professionally accountable for their actions
- there is clear evidence that some clinics/practitioners in the sector are envisaging using and promoting herbal medicine for the treatment of serious medical conditions. The MHRA has seen various clinic leaflets and websites (including UK based ones) promoting herbal medicine for the

treatment of, and as having efficacy in, serious conditions. It is essential to public safety that practitioners should know the limits of their own competence and should be operating within clear parameters. Public health risk can arise if patients are misdiagnosed, if they delay seeing a doctor for a serious medical condition, are encouraged to give up or reduce prescribed medication without taking advice from a doctor, or are taking a mixture of herbal and conventional medicines without expert supervision

- historically, levels of adverse drug reaction (ADR) reporting for herbal medicines have been low. This reflects many factors, not least that survey evidence shows that often patients do not tell their doctor that they are taking herbal medicines. Typically the MHRA has received about 60-70 ADR reports a year. However, the introduction of patient reporting via the yellow card scheme may well have a significant effect. Between 1 January and 30 September 2006 the MHRA received 63 reports of which 34 were from health care professionals and 27 were from patients

Evidence of poor practice by practitioners putting patients at risk

- there have been various examples of poor professional practice; some are implicit in points covered above, eg:
    - practitioners/clinics deliberately or carelessly tapping into the international trade in low grade products
    - practitioners sourcing products from uncontrolled sources, such as relatives abroad

- practitioners/clinics have regularly been found using advertising leaflets that make unsubstantiated claims about safety eg that medicine from a particular tradition has no side effects or is safer than western medicine. The external manifestation can be dealt with, eg the public or reputable practitioner organisations could refer misleading advertising to an appropriate regulatory body, such as the Advertising Standards Authority. However, the underlying issue remains that there is a strong case for practitioners being fully professional accountable for their knowledge of safety issues and for the advice they are giving to patients

- MHRA is aware of various other reported concerns, not least within the herbal medicine profession itself, that some practitioners have qualifications of doubtful value; that some practitioners cannot communicate effectively in English; and that some practitioners hold consultations that are cursory and do not include checking previous medical history and what other medication is being taken. A number of these issues have been the subject to scrutiny by the investigative media.

8. Overall, a programme to establish systematic regulatory arrangements for s12(1) is fully consistent with the strategy for improving the regulation of herbal medicine advocated by WHO and with the direction of international developments.

<u>Principles of better regulation</u>

9. The five guiding principles of better regulation identified by the Better Regulation Task Force are:

    - proportionality
    - accountability
    - consistency
    - transparency
    - targeting.

10. The MHRA would welcome views on how the various proposals accord with the principles of better regulation. This issue is challenging given that s12(1) reforms would be seeking to achieve effective regulation in a hitherto largely unregulated situation where a wide variety of practices have grown up. It would also be helpful, where interested parties favour an alternative approach, if they could identify how these alternatives would more effectively comply with the principles of better regulation.

    Alternative approaches to improving standards

11. The MHRA's developing proposals, as outlined in a series of informal discussion papers, are based on combining the following approaches:

    - updated and more systematic **medicines legislation**
    - all **practitioners operating under s12(1) to be professionally accountable**
    - **codes of practice agreed with the profession**.

12. An alternative approach would be one in which involved:
    - some limited improvements to medicine legislation
    - codes of practice agreed with those s12(1) operators who chose to submit to arrangements for professional accountability
    - it remaining legally possible for practitioners to operate under s12(1) even though they were not part of any process of professional self regulation
    - the public to be given information to enable them to make an informed choice between practitioners who had opted for professional accountability.

13. The MHRA has concerns about this second approach; arguably, it would not protect public health adequately, would lead to an adverse incentive for those practitioners seeking to follow high standards and would be likely to undermine rather than support attempts by responsible practitioners to achieve and maintain consistent high standards. It would put vulnerable members of the public at the risk of being taken advantage of by poorly trained and unaccountable practitioners who had chosen to opt out of initiatives to improve professional regulation. The Agency also doubts that this approach would lead to long term stability in the herbal medicine sector. By undermining general public confidence in standards in the herbal medicine sector it would also be likely to have an adverse regulatory impact on

companies that had invested to meet the high standards required by the THR scheme.

Industrial production

14. The MHRA has been asked on a number of occasions whether it would be possible to define the concept of industrial production so that interested parties could be clearer on whether particular types of activity legitimately fell within the s12(1) provision or should more properly be subject to the requirements of Directive 2001/83/EC, as amended. The MHRA currently doubts that it would be feasible to draw up detailed guidance or legislation on the circumstances in which a medicine is "neither prepared industrially nor prepared using an industrial process" - this is an issue which affects the regulation of many other medicines besides herbal medicines. However, MHRA will remain alert during discussion on the possible reforms of s12(1) (and, as applicable, to their subsequent implementation) to the possible need for guidance or legislation to circumscribe the operation of s12(1) to take account of this concern. This might be necessary if it became clear that the provision might be used, or was being used, in ways that risked undermining the legal basis of the s12(1) scheme.

Issues for discussion

15. Several key questions are set out below. Other more specific questions arise from the other discussion papers.

Issues for discussion

- ***What is your current assessment of the case for regulation?***
- ***Do you agree on the central importance of requiring systematic professional accountability for those who wish to benefit from the exemption in s12(1)?***
- ***Do you agree that best overall approach to improving s12(1) would be through a combination of updated medicines legislation and agreement with the profession on codes of practice? If not, what approach do you advocate and why?***

How to comment on these documents

Any written comments on the proposals should be sent by 30 March 2007 to Caroline Brennan at the MHRA, Market Towers, 1 Nine Elms Lane, London SW8 5NQ. The E mail address is: caroline.brennan@mhra.gsi.gov.uk.

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