Over the counter medicines: proceed with caution

Robin Ferner and **Keith Beard** caution that the risks of increasing people's access to over the counter medicines may outweigh the benefits

An all party parliamentary group in England is currently assessing whether there is a case for banning over the counter access to analgesics containing weak opioids.¹ Recent coroner's inquests found that a 41 year old man died from respiratory depression after taking an over the counter analgesic containing paracetamol and dihydrocodeine² and attributed the death of a 49 year old woman to renal failure from addiction to an over the counter preparation containing ibuprofen and codeine.³ Here we consider what determines whether a medicine is available over the counter and whether changes are needed.

Current legislation

UK legislation to regulate the supply of medicines dates back 40 years. It stems from the disastrous consequences of prescribing the teratogenic drug thalidomide to pregnant women after inadequate safety checks.⁴ The ensuing inquiries led to the UK Medicines Act 1968⁵ and European Economic Community Directive 65/65/EEC.⁶ Broadly, these divide medicines into classes that do or do not require prescription (see table 1 on bmj.com). In Europe and the United States, a newly licensed medicine will usually be available only on prescription. In much of the developing world, however, licensed medicines are available without prescription.

Regulation by prescription is no guarantee of prudent use. For example, an especially virulent strain of

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methicillin resistant *Staphylococcus aureus* is now common in patients presenting to emergency rooms in the United States⁷—a probable consequence of widespread overuse of antibiotics—and the emergence of a resistant *Streptococcus* has led to calls to restrict the use of levofloxacin.⁸ Nevertheless, prescription only medicines are subject to a range of controls that are relaxed when medicines are made more freely available over the counter. These controls may limit the opportunity for indiscriminate use but also limit people's involvement in decisions about their health, including the medicines they take.

Balance between benefit and harm

Medicines regulators must determine if a medicine should be available, and if so, whether it should be by prescription only or over the counter. They decide whether to grant a marketing authorisation for a drug by assessing whether it is effective and of good quality, and if so, whether it is acceptably safe relative to its likely benefits. Different regulators reach different decisions (see table 2 on bmj.com).

When deciding if a medicine should be reclassified to make it available over the counter, regulatory authorities must balance the benefits of easier access against the potential harm from unsupervised or inappropriate use. Some countries have an intermediate stage, pharmacy only sale, where there is still some supervision from healthcare professionals. Once medicines have been reclassified, they remain subject to safety review. Safety concerns can emerge with continued use and restraints need to be reimposed. In the UK, the antihistamine terfenadine was reclassified from prescription only to pharmacy status, only to be switched back again when its propensity to cause torsade de pointes was appreciated.⁹

In favour of wider availability

Patients potentially benefit in several ways if medicines are available over the counter. They can call at any pharmacy rather than waiting for an appointment with a general practitioner. They can treat their common and troublesome conditions with easily recognised symptoms, such as hay fever and cold sores. Importantly, they can easily obtain treatments—for example, post-coital contraception—that have to be taken quickly to be beneficial.¹⁰

Others benefit too. Hard pressed general practitioners no longer need to write prescriptions for minor ailments. Pharmacists, latterly reduced to handing out pre-packaged tablets, can make better use of their

In China, many licensed drugs don't need a prescription

professional skills. And because patients pay directly for the medicines they buy over the counter, spending on medicines by insurers and central government falls.

Drug companies and retail pharmacies can expect to benefit commercially from reclassification of medicines as over the counter. Companies often seek reclassification around the time that a patent expires.¹¹ Applications for over the counter medicines may be slow because it takes time to accrue sufficient information to show acceptable safety, but the large reduction in price that can occur after a patent expires, the large potential market for pharmacy only medicines, and the fact that they can be advertised directly to consumers may be incentives too. In the US and New Zealand, where direct to consumer advertising of prescription only medicines has been allowed, the evidence points to a strong influence.¹² Licences for over the counter sales can certainly boost the share price of big drug companies.¹³

Concerns about wider availability

The use of inappropriate medicines is clinically unwelcome because it exposes the taker to harm without any prospect of benefit and may be disadvantageous in other ways. The UK Medicines and Healthcare Products Regulatory Agency authorised the use of low dose simvastatin without prescription, despite fears that over the counter statins would be misused.¹⁴ Increasing antimicrobial resistance reminds us of the dangers to global public health of unfettered prescribing.¹⁵

There are other worries about over the counter medicines. A patient who makes the wrong diagnosis and uses an inappropriate over the counter medicine, may present late with a potentially serious but treatable condition. Prescribers also have no opportunity to reinforce instructions for safe use as they can with prescribed medicines. Certainly, pharmacists can provide clinical advice to minimise the risk of misuse of pharmacy only drugs, but supervision by a busy community pharmacist in the UK may be perfunctory. As the UK regulatory agency notes: "You will see the sale assistant show the medicine to the pharmacist when you buy it."¹⁶ Rare but important adverse effects may become manifest, and be attributed correctly, only after many patients have taken a drug. The association between aspirin, first marketed in 1899, and Reye's syndrome was suggested only after 80 years of use.¹⁷ There is therefore always residual uncertainty about the safety of medicines.

Several potential strategies can improve the safety of over the counter medicines. If the safety margin is too narrow, if self diagnosis is unreliable, or if there are unresolved safety questions, regulators can reduce the potential for harm by specifying the concentration, dose, or pack size that a pharmacist can supply without prescription.¹⁸ For example, omeprazole can be supplied over the counter as 10 mg tablets with a maximum daily dose of 20 mg¹⁹ and the pack size of paracetamol that can be bought over the counter is greater in a pharmacy than in a supermarket. This strategy probably does reduce harm: fewer patients have been admitted with, or died from, paracetamol

Number of drugs switched from prescription only medicine to pharmacy medicine in UK by year.²³ Data for 2006 were incomplete

poisoning since the pack size was reduced.^{20 21} Nevertheless, the imposition of lower doses for over the counter medicines is unlikely to ensure benefit: drugs like omeprazole or simvastatin are probably less effective in low doses than in the higher doses usually prescribed.

There are also disadvantages when relatively safe and effective analgesics such as paracetamol and ibuprofen are combined with small doses of opioids that are likely to bring trivial therapeutic benefit but increase the risks of abuse, addiction, and adverse effects. Co-proxamol, a combination analgesic containing paracetamol and the opioid dextropropoxyphene, was withdrawn from the UK market because evidence of increased analgesic efficacy was lacking, while there was good evidence of increased harm.²²

Regulatory action can make drugs more widely available while guarding against these difficulties. The government was optimistic that legislation in 2002 would substantially increase the number of medicines available without prescription,²³ but progress has been modest, perhaps reflecting a cautious approach (figure).

Attempts to restrict the availability of medicines face a much greater problem. Internet shopping now makes it straightforward, if risky, to order medicines without involving a doctor or pharmacist in the decision. The Royal Pharmaceutical Society of Great Britain estimates that two million Britons obtain their medicines that way.²⁴

Steps to increase safety

Both overuse and underuse of effective medicines can cause serious harms. The benefits of self treatment probably apply to only a small subset of medicines. There is little evidence in the UK that the current policy governing the change from prescription only to over the counter medicines has exacerbated the harm of overuse. Although we can take heart from the fact that major disasters such as thalidomide have been avoided by stringent licensing regulations, the global outlook is rather more sombre. Much of the world has little or no effective regulation of medicines once licensed, and the internet makes these medicines, or counterfeit versions of them, available worldwide. The Royal Pharmaceutical Society

proposes a “seal of approval” for legitimate internet pharmacies, but many people seem prepared to risk fake drugs, often for erectile dysfunction or obesity, rather than confide in a prescriber and present the prescription at a recognised pharmacy.²⁴ The society’s initiative is unlikely to plug the internet loophole, and we face the uninviting prospect that medicines regulation will become ineffective everywhere.

The safety of over the counter medicines has to be continually reviewed, even though this is difficult in practice. Since healthcare professionals may not be involved, we have to rely on patients to report adverse effects. The UK regulatory agency’s new simplified yellow card system inviting patients to report adverse drug reactions could therefore be helpful.²⁵ When safety concerns are raised regulators should investigate. Since efficacy is also important, regulators should ask for clearer evidence of benefit at the over the counter dose if this is lower than the dose usually prescribed. Given the concerns, it would be wise to avoid any wholesale rush to reclassify medicines. Whole communities might lose out in the long run if indiscriminate overuse of widely available medicines were to lead to large numbers of avoidable but irreversible adverse effects.

Contributors and sources: KB and REF have both been interested in rational prescribing, adverse drug reactions and pharmacovigilance for many years. This article arose from discussions with a *BMJ* editor and was modified in the light of comments from Philip Routledge and Silvio Garattini, who reviewed an early version. Both authors drafted the article, revised it, and approved the final version for publication. They are both guarantors.

Competing interests: KB is a member of advisory committees at the Medicines and Healthcare Products Regulatory Agency (MHRA) and of the pharmacovigilance working party of the European Committee of Medicinal Products for Human Use. REF is a member of MHRA advisory committees. The views expressed here do not represent the views of the MHRA or its committees.

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SUMMARY POINTS

Cautious reclassification of medicines to allow over the counter sales seems safe

The doses of some drugs available over the counter are unlikely to be optimally effective

The safety of over the counter medicines should be kept under review

Patient reporting of adverse drug reactions may help

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CORRECTIONS AND CLARIFICATIONS

Systemic lupus erythematosus

In this *Pregnancy Plus* article by Lucy H Mackillop and colleagues (*BMJ* 2007;335:933-6, 3 Nov, doi: 10.1136/bmj.39358.519491.AD), we added a short “standfirst,” an editorial device used at the start of some articles to give the reader an idea of what the article is about. This standfirst implied that systemic lupus erythematosus should not be treated in pregnancy, whereas the reverse is true. The article makes this clear.

Obituary: John Edgar Morison

In this obituary we inexplicably published the name of the first author as Chris Morison, when in fact his name, as he had clearly supplied to us, is John Morison (*BMJ* 2007;335:999, 10 Nov, doi: 10.1136/bmj.39379.678356.BE).

Investigating progressive unexplained renal impairment and hypertension

In this *Practice* article by LA Ratnam and colleagues, we failed to spot that the unit for creatinine concentration was wrong (*BMJ* 2007;335:1094-6, 24 Nov, doi: 10.1136/bmj.39363.672743.AD).

Throughout the article, the values given for these concentrations were correct, but the unit should have been $\mu\text{mol/l}$ [not mmol/l].

Minerva

Slipping from her usual standard of excellence, Minerva made a sad hash of the second item on her page of the issue of 15 September (*BMJ* 2007;335:570, doi: 10.1136/bmj.39332.450845.471). For an accurate and comprehensible summary of the work of Hessel et al (*Nature* 2007;449:101-4), we can do no better than to direct you to Chris Smith’s exemplary explanation in his Rapid Response of 18 September (www.bmj.com/cgi/eletters/335/7619/570?ck=nck#176716).

Number of serious adverse events doubles in seven years in US

In seeking to add value to the print version of this *News* story by David Spurgeon (*BMJ* 2007;335:585, 22 Sep, doi: 10.1136/bmj.39339.624711.DB), our *News* team cunningly found out which drug came out top of the list for adverse reactions. Unfortunately, they also managed to misspell it, in the text and figure caption, as “oxycondone.” It should, of course, be oxycodone.