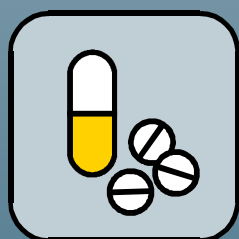


Understanding and Responding to Pharmaceutical Promotion

A Practical Guide

First edition

Working Draft for Pilot Field Testing



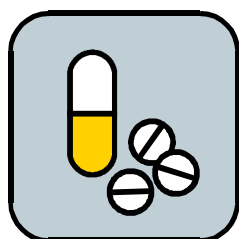
World Health Organization/Health Action International
Collaborative Project

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Preface

Medicines can play a crucial role in the attainment or maintenance of health but it is vital that they are used rationally. If a patient needs treatment, he or she must have access to the right medication, in the right dosage and for the appropriate course of treatment. Health-care professionals, such as doctors and pharmacists, play a key role in ensuring that medicines are used appropriately. As gatekeepers to care, they need to assess different treatment options, including pharmacotherapy, and consider each for potential benefit and harm.

In 1994, the World Health Organization (WHO) published the *Guide to Good Prescribing*. This publication was developed and field tested extensively before its release. After publication, it was translated into multiple languages and was widely used. This guide highlighted the need for students to learn to focus in a very practical way on treatment goals when making prescribing decisions, and to develop their own personal formulary for commonly treated conditions. The report of the evaluation was published in *The Lancet* (1995).

However, in recent years, growing concern has focussed attention on the relationship between health-care professionals and the pharmaceutical industry - particularly the industry's influence on prescribing and dispensing decisions through a range of promotional tools, which can influence treatment choices. This influence can lead to less than optimal medication choices, sometimes to the detriment of patient health.

Despite the fundamental nature of these treatment decisions and the important role of pharmaceutical promotion in shaping them, health-care professionals receive little or no instruction on how to assess pharmaceutical promotion and how to understand its often subtle influence on their behaviour. In 2005 a WHO/Health Action International (HAI) cross-sectional, international survey of educational initiatives on pharmaceutical promotion found that whilst many medical and pharmacy faculties included this topic in their curriculum, most spent less than one day on the subject - with some schools devoting only one to two hours to the issue. The survey also showed that even though educators recognise the need for instruction on pharmaceutical promotion and sometimes do their best to incorporate it into their work, it is mostly limited. There is, therefore, both an identified need and an expressed determination by educators to further develop curricula in this area.

This new publication is modelled on and should be seen as a companion module to the *Guide to Good Prescribing*. It will assist teachers and health-care professionals to teach medical and pharmacy students about pharmaceutical promotion. *Understanding and Responding to Pharma-*

ceutical Promotion – A Practical Guide has been produced as part of a collaborative HAI/WHO project focusing on pharmaceutical promotion and its effect on the rational use of medicines in many countries around the world. It has been made possible thanks to the expertise and knowledge of numerous WHO and HAI staff members and a broad group of educators and activists working with the HAI network on pharmaceutical promotion.

This draft manual is a first step in addressing the need for medical and pharmacy professionals to reconsider their central role as a target for pharmaceutical marketing and to provide some understanding of how this fits into the wider context of promotion. Its nine chapters explore a spectrum of related topics that will help them be better prepared to face the promotional activity to which they will be exposed and to analyse information about medicines in order to make choices that will contribute to the health of patients.

We do not consider this to be the final product. We encourage feedback on the material included in this book so that it can be improved and updated as it is vital that this publication reflects the real needs of students and educators. The manual will be rigorously pilot tested and evaluated at a number of sites during 2009-2010 using English and Spanish versions of the text. Afterwards, it will be revised following close examination of feedback and evaluation data. In addition, classroom experiences using this text and its exercises will be collected in order to revise the material for wider use in the future. We hope that the manual provides material for thought-provoking discussions and we look forward to receiving your comments.

Hans Hogerzeil

Director

ESSENTIAL MEDICINES AND PHARMACEUTICAL POLICIES

WORLD HEALTH ORGANIZATION

Geneva

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HEALTH ACTION INTERNATIONAL GLOBAL

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Abbreviations and Acronyms

ABPI	Association of the British Pharmaceutical Industry
ARR	Absolute Risk Reduction
CLASS	Celecoxib Long-Term Arthritis Study clinical trial
CME	Continuing Medical Education
DDMAC	US Food and Drug Administration's Division of Drug Marketing, Advertising and Communication
DTCA	Direct-to-Consumer Advertising
FDA	US Food and Drug Administration
HAI	Health Action International
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
INN	International Nonproprietary Name
KOL	Key Opinion Leaders
NNT	Number Needed to Treat
PhRMA	Pharmaceutical Research and Manufacturers of America
ROI	Return on Investment
RRR	Relative Risk Reduction
Rx&D	Canada's Research-based Pharmaceutical Companies
UK	United Kingdom
US	United States of America
VIGOR	Vioxx Gastrointestinal Outcomes Research clinical trial
WHO	World Health Organization

Chapter 3

Analysing pharmaceutical advertisements in medical journals

Joel Lexchin

Although the pervasive presence of pharmaceutical advertisements in medical journals may suggest otherwise, companies only spend a small fraction of each promotional dollar on advertisements. US figures from 2005 show that medical journal advertising cost companies US\$499 million out of a total promotional budget of US\$27.7 billion (IMS, 2005). Journal advertising is used with visits from sales representatives and detailing aids (material left behind by sales representatives) to deliver and reinforce a message about a medicine. According to an executive from the research organisation that has undertaken the most extensive media research on the prescription medicine industry: “*Advertising magnifies the detailing effort at a fraction of detailing expense. In effect, detailing provides the power in the marketing effort and advertising provides the efficiencies.*” (Liebman, 2000). For every dollar spent on medical journal advertisements during the first four years that a medicine is on the market, the return on investment (ROI) is US\$2.43; after this time, ROI increases to over US\$4.00 (Liebman, 2000).

Not only are journal advertisements successful in increasing sales, and therefore prescriptions, but there is also some evidence that physicians who use journal advertisements as an information source prescribe less appropriately (Bower, 1987; Ferry, 1985).

Journal advertisements attract attention because they are visually appealing. Professionals may also see them as a way of keeping up-to-date. Since advertisements can affect prescribing, it is important to be able to critically evaluate their contents and to compare the information provided with that obtained from unbiased information sources.

Aims of this chapter

By the end of the session based on this chapter, you should:

- Know what kinds of information the WHO *Ethical Criteria for Medicinal Drug Promotion* recommend for inclusion in journal advertisements;
- Be familiar with the different components of journal advertisements;
- Understand the ways in which each of the components can be used to convey messages;
- Be able to evaluate each of the different components according to the criteria set out in this chapter.

What information should be in a journal advertisement?

The *Ethical Criteria for Medicinal Drug Promotion* developed by the World Health Organization (WHO) suggest the types of information that, as a minimum, should be contained in a journal advertisement (WHO, 1988), (see Box 1). The aim is to ensure that basic information needed for prescribing decisions is present. The medicine's international nonproprietary name (INN), usually the generic name, is a key piece of information that should always be included. Generic names help doctors and pharmacists identify which class a medicine belongs to and can prevent doctors from unknowingly prescribing two medicines from the same class to a patient.

Box 1: Recommended information in journal advertisements

The World Health Organization's Ethical Criteria recommend that the following information be included in pharmaceutical advertisements appearing in medical journals.

- Name(s) of the active ingredient(s) using either international nonproprietary name (INN) or the approved generic name of the medicine;
- Brand name;
- Content of active ingredient(s) per dosage form or regimen;
- Name of other ingredients known to cause problems;
- Approved therapeutic uses;
- Dosage form or regimen;
- Side effects and major adverse medicine reactions;
- Precautions, contraindications and warnings;
- Major interactions;
- Name and address of manufacturer or distributor;
- Reference to scientific literature as appropriate.

(WHO, 1988)

While advertisements from developed countries typically contain nearly all of the information listed in the box, this is not always the case in developing countries. Table 1 from a 1993 study presents the results of a survey comparing advertisements in developed and developing countries. It is obvious from examining this table that safety information is systematically ignored in advertisements from developing countries. More recent work analysing advertisements in India (Lal, 1997; Lal, 1998), Brazil (Mastroianni, 2005) and the Russian Federation (Vlassov, 2001) shows that they continue to leave out essential information recommended by WHO.

Table 1: Information in advertisements in developed and developing countries

Type of information	Percentage of advertisements containing information	
	Developed countries*	Developing countries**
Indications	89	87
Contraindications	61	28
Warnings	55	29
Side effects	64	29

(Herxheimer, 1993)

* Denmark, Finland, France, Ireland, Italy, Norway, Spain, Sweden, Switzerland and United Kingdom

** Brazil, Indonesia, Nepal, Pakistan, Sri Lanka, Turkey, United Republic of Tanzania and Zimbabwe

Just because each of the categories of information is present in an advertisement does not necessarily mean that the advertisement will give a complete picture of the medicine's safety and effectiveness and how to prescribe the medicine appropriately. Although advertisements in Australian journals improved during the 1980s and early 1990s, by 1992, 4% still contained unacceptable graphics, 7% had unacceptable claims and 15% had unacceptable references (Carandang, 1994). In 1992, the *Annals of Internal Medicine* published an article that critically examined the scientific accuracy of over 100 pharmaceutical advertisements in 10 leading medical journals (Wilkes, 1992). Overall, physician and pharmacist reviewers judged that 34% should have had major revisions before being published and 28% should not have been published at all. In 1995, most Irish doctors expressed strong reservations about the quality of advertisements in Irish medical journals, with 90% believing that the advertisements were of poor educational value (Hemeryck, 1995).

Figure 1: What information should a medicine advertisement contain?



(Advertisement from the *Indian Journal of Dermatology, Venereology, Leprology*. Vol 71, Issue 6, Nov-Dec 2005.)

The main components of advertisements

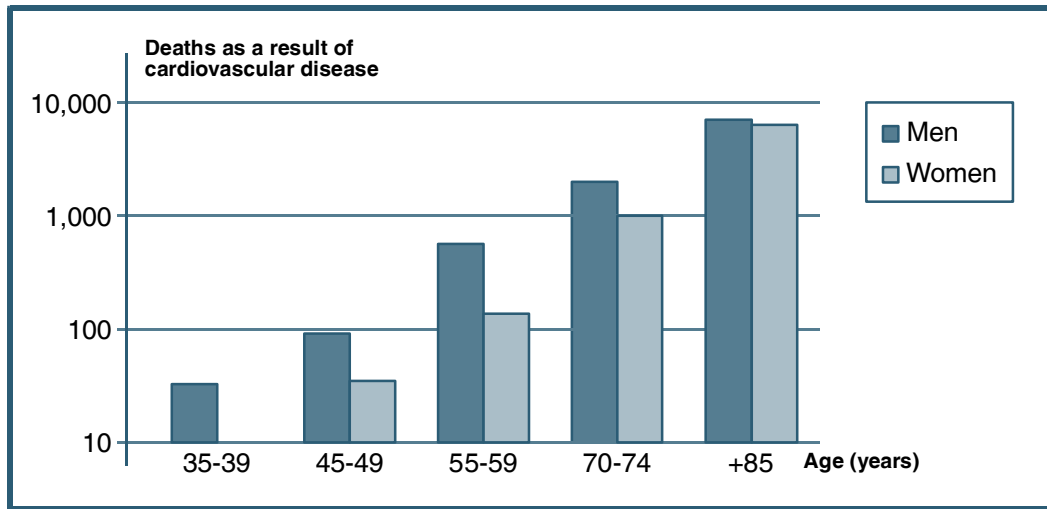
This chapter will consider four main elements of journal advertisements: graphs and data; text; references; and pictures and images.

Graphs and data

Graphs and data are often used in advertisements to provide a scientific justification for the claims that are being made about a medicine. A graph can provide a clear, visually striking summary of study results. However, an analysis of 74 graphs that appeared in 64 advertisements in leading US medical journals found that 8% had errors, 5% were visually confusing and 12% used non-standard graphing techniques. Only 36% of graphs were self-explanatory and there were many more visual distractions and numeric distortions than in graphs found in medical journal articles (Cooper, 2001).

Figure 2 presents an example of a graph on a promotional website with one type of numeric distortion (for details, see caption below figure). There are many other types of examples, including not starting a scale at zero, making a very small difference in outcomes look large, highlighting one small part of a study's results and so on.

Figure 2: What is numeric distortion? An example



(Source: Bayer, Schering Pharma, 2009)

This graph appeared on a website on menopause by Schering, which markets post-menopausal hormone treatments: <http://www.menopause-infoline.com/scripts/en/consumer/index>. and http://www.menopause-infoline.com/scripts/en/consumer/01/c_01_04_02.php. The graph accompanies text that stresses the increase in heart disease risk faced by women as they age.

The y-axis, on the left, is a logarithmic scale, an unusual scale to use on such a graph. Readers glancing at the graph might assume the scale was arithmetical, with equal numbers between the horizontal lines. For example, if one glances at the bars for ages 70-74, it looks like nearly as many women as men are represented. In fact, the bar represents 1,000 deaths among women versus 2,000 among men.

Data on medicine benefits and harmful effects

Closely related to the issue of the quality of graphs is whether advertisements convey information as a relative risk reduction (RRR), absolute risk reduction (ARR) or number needed to treat (NNT).

A **relative risk reduction** is the percentage reduction in the risk of targeted complications between two groups. A drop in mortality from 2% to 1% would be a RRR of 50%, because 1%, or 1 in 100 people, is half as many as 2%, or 2 in 100 people. An **absolute risk reduction** is the absolute percentage difference in the risk of targeted complications between two groups. A drop in mortality from 2% to 1% would be an ARR of 1%. The **number needed to treat** is the number of patients who have to be treated in order to provide the desired effect from the medicine in one person. A drop in mortality from 2% to 1% would be a NNT of 100 (ARR=1; NNT=100/ARR). In other words, for every death prevented, 100 people would need to be treated. There is evidence that physicians' enthusiasm for a treatment varies depending on how the results are presented. Specifically, the inclination to use a particular medicine therapy is greatest when

results are given as a RRR and lowest when they are given as a NNT (Cranney, 1996; Naylor, 1992). A 50% relative reduction looks much more impressive than a 1% absolute reduction. Often the word ‘relative’ is not stated, adding to the confusion. (Chapter 8 describes these outcome measures in greater detail.)

Figure 3: Misleading use of relative risk reductions



(Advertisement brochure from Alonso, 2007.)

This advertisement for raloxifene (Evista) is an illustration of a brochure distributed by sales representatives to family physicians in Spain. Raloxifene is approved in Spain to prevent fragility fractures in women with osteoporosis. The advertisement was judged by regional medicine authorities in Madrid to be illegal because it promotes an unapproved use. The lower box with the large “75%” is promoting use in women without a diagnosis of osteoporosis (“75% reduction in vertebral fractures in women with osteopaenia”) (Alonso, 2007).

Impressive risk reductions, but what do they really mean?

47% relative risk reduction in radiological vertebral fractures

- A radiological vertebral fracture is not a broken bone in the traditional sense as the woman has no symptoms. It is a loss in vertebral height seen on x-ray. The cut-off for the amount of loss in height considered to be a fracture is arbitrary, and is 15% in some studies, 20% in others, including this study.
- What is the absolute risk reduction? Over 3 years, 6% of women on raloxifene had radiological vertebral fractures versus 10% on placebo, a 4% difference.
- Numbers needed to treat: 25 women must be treated for 3 years to prevent one radiological vertebral fracture. However, only a difference on x-ray would be prevented, not pain or disability.

75% relative risk reduction in symptomatic vertebral fractures

- These x-ray changes led to back pain and were therefore clinically meaningful.
- In total, less than 1% of women had clinical vertebral fractures in 3 years. No breakdown is provided of numbers on raloxifene versus numbers on placebo.
- The published report does not allow ARR to be calculated – a guess from the relative risk reduction figures and total number of women is around 0.7%.
- In the same cited study, 1% of women on raloxifene developed venous thromboembolism (deep vein thrombosis or pulmonary embolism) compared to 0.03% on placebo; absolute risk increase = 0.7% (Ettinger, 1999).

A Canadian study that looked at 22 journal advertisements found that half of the time, in 11 of these advertisements, results were reported only as a RRR. The other 11 provided enough information to calculate ARR and NNT, however, they did not state these values directly (Lexchin, 1999). Australian advertisements that made claims explicitly reporting quantitative outcomes also did not report data as either the ARR or NNT (Loke, 2002).

Advertising copy cannot contain all the methodological and statistical detail found in the original reports but it should allow readers to know if the research being cited meets the basic criteria for validity, significance of results and applicability to the reader's practice (Rothermich, 1996). Gutknecht analysed 43 data presentations in 33 advertisements that contained quantitative research results. References to randomisation and blinding were found in less than one-half of the 43 data presentations. *P* values (the probability that a specific result occurred by chance) were frequently provided, but confidence intervals and references to power and NNT were not

provided in any of the advertisements (Gutknecht, 2001). Similarly, a study of Finnish advertisements found that these adverts failed to mention confidence intervals or NNT (Lankinen, 2004).

Box 2: How to evaluate data and graphs presented in pharmaceutical advertisements

- Is information presented as either absolute risk reductions (ARR) or number needed to treat (NNT)?
- Does the advert indicate if a study was randomised and blinded?
- When statistical significance is given are confidence intervals and power calculations included?
- Are graphs simple to read and do they have appropriately labelled axes?
- Are graphs obscured by other visual material?
- Are the titles of graphs clear and do they explicitly say what the graph is about?
- If the graph comes from an article or another source is it reproduced exactly as it appeared in the original source?
- Are data in graphs presented in such a way as to make it easy to determine whether or not any differences are clinically meaningful?

Advertising text

• Claims made in advertisements

One of the essential features of a journal advertisement is the product claims. These claims can take many forms. They may be about effectiveness, safety, enhancement of quality of life, or sometimes costs or convenience. Sometimes a precise claim is made about a measurable treatment outcome; other times claims are much more vague.

The claims made in a sample of 245 advertisements from four major Finnish medical journals published in 2002 were examined (Lankinen, 2004). These claims were classified into four groups: unambiguous clinical outcome, vague clinical outcome, emotive or immeasurable outcome and non-clinical outcome. Out of 883 claims only 337 (38%) were referenced. Nine percent of the claims implied unambiguous clinical outcomes, 68% included vague or emotive statements. Twenty-one percent of the references were irrelevant to the claim. There was a fair amount of non-scientific and scientific support for the 73 unambiguous claims, but not a single

claim was supported by strong scientific evidence (meta-analysis or multiple high-quality studies). Vague, emotive and non-clinical claims were significantly more often supported by irrelevant references than unambiguous claims.

Advertisements from medical journals in other countries are little different from those in Finland with respect to whether or not they contain supporting information. Only 45% of 855 claims in Australian advertisements were supported by compelling evidence (randomised, controlled trials or better) (Loke, 2002). A review of Spanish advertisements found that 44% of claims for which a reference was cited were not supported by the referenced studies. Usually this was because the advertisement recommended the product for a patient group that was not included in the study (Villanueva, 2003).

• **Quality of life claims**

Quality of life claims may reflect one or more of three dimensions: physiologic, functional (physical, social and psychological functioning) and overall well-being. Advertisements most often claim that the product improves quality of life in either the physiological or physical functioning dimensions. In a US review of these claims (Rothermich, 1996), 11 out of 26 advertisements (42%) making claims about quality of life were non-compliant with US Food and Drug Administration regulations, mainly because of biased information presentation, with too much prominence given to medicine benefits as compared to harmful effects.

• **Claims about costs and economic benefits**

Doctors often do not know the relative costs of the medicines they prescribe, but they may try to prescribe lower-cost medications to low-income patients and those without medicine insurance (Ryan, 1990; Safavi, 1992). Therefore, it is not surprising that economic messages in advertisements typically claim that a medicine is “less expensive” than alternatives. One study of such advertisements found that simple cost differences were usually supported by evidence, but most claims of cost-effectiveness or of positive effects of the treatment on patients’ productivity were not supported by evidence (Neumann, 2002). Inaccurate or deceptive information about economic benefits could lead to doctors prescribing more expensive medicines that do not offer any clinical advantages.

• **Efficacy and safety claims**

Claims about clinical outcomes are important since this is the key aim of pharmacotherapy. Table 2 summarises the types of claims in Australian and Finnish advertisements and shows that in both countries only a minority of the claims are about unambiguous clinical outcomes (Loke,

2002; Lankinen, 2004). A significant proportion is emotive, for example, “one of a kind” or “a source of healing power”, and almost a quarter are for non-clinical outcomes which are usually about surrogate markers, such as changes in laboratory measures or physiological measurements, rather than meaningful clinical changes in morbidity events or mortality. Surrogate end points may or may not correlate with outcomes that are important to patients.

Whatever the nature of a claim, it should be presented clearly, should be based on methodologically strong research and should accurately reflect cited references. Ideally, claims should also reflect treatment outcomes of importance to patients’ health and lives.

Table 2: Types of claims in pharmaceutical advertisements

	Unambiguous clinical outcome		Vague clinical outcome		Emotive or immeasurable outcome		Non-clinical outcome		Total number of claims
	No.	%	No.	%	No.	%	No.	%	
Australia	418	28	437	29	301	20	346	23	1,504
Finland	81	9	326	37	270	31	206	23	883

(Source: Loke, 2002; Lankinen, 2004)

References in advertisements

Advertisements should include references whenever a claim is made that reflect scientific evidence. The claim must be consistent with cited research and the research should be designed with adequate methodology. For example, effectiveness claims should generally be based on evidence from double-blind, randomised, controlled trials. It is also important for health professionals to be able to retrieve cited references, so that they can independently evaluate them. Otherwise, any limitations or inconsistencies between the evidence and the claims will remain hidden.

These are a few common problems with referencing in advertisements:

- No references are provided for claimed treatment effects;
- Reference is to company “data on file”, which is not publicly available and has not been independently reviewed;
- A poster presentation is cited; generally inadequate information is provided on methods in poster presentations to judge reported results;

- Review articles that selectively present results are cited, not original research;
- The referenced article is in a journal supplement sponsored by the manufacturer;
- Study results in the cited reference are inconsistent with the advertising claim;
- The study is of poor methodological quality, raising questions about the validity of the results.

For example, Lexchin and Holbrook requested all references for a set of published advertisements, 87 in total, from the manufacturers (Lexchin, 1994). Ten of these references were to unpublished “data on file”. They eventually received 90% of the requested references; 4 of the 10 “data on file” were not sent. Although 76% of the references supported cited claims, the overall methodological quality of the references was judged to be unacceptably low (Lexchin, 1994).

In a similar study, Villanueva and colleagues (2003) retrieved 82% (102 out of 125) of references cited in advertisements. However, almost half of the references that were not found were to “data on file”. Over three-quarters of the references came from journals with a high impact factor (a measure of how often articles in a journal are cited) and 82% of the 102 were from randomised clinical trials.

In another analysis of references in advertisements, Cooper and Schriger (2005) only received 37 replies to 88 requests for cited “data on file”, 19 of which were refusals; only 18 (20%) were provided. Out of 294 references citing original research, 58% were sponsored by or had authors affiliated with the product’s manufacturer. When pharmaceutical companies sponsor research on their products, the results are four to five times more likely to be favourable to the product than when financing is from other sources (Als-Nielsen, 2003; Lexchin, 2003). Finally, in developing countries it may not be possible to retrieve references because the information in citations is incomplete. This was the case 90% of the time in one study in India (Lal, 1996).

Box 3: How to evaluate references in pharmaceutical advertisements

- Do citations contain all of the information necessary to identify references?
- Are all references cited retrievable including those to “data on file”?
- Are references of high methodological quality?
- Do journal references come from peer-reviewed medical or pharmacy journals?
- Did the company finance the research reported in the reference?

• **Claims in antibiotic advertisements**

Advertisements for antibiotics raise specific concerns, as overuse of antibiotics can lead to resistance and diminish the usefulness of these medicines. Many advertisements for antibiotics do not mention resistance (Gilad, 2005). In some cases, as in the advertisement shown in Figure 4, advertisements fail to state that a common infection usually resolves without antibiotics or that it is often wiser to reserve newer broad-spectrum antibiotics for second-line use, when older narrower-spectrum products fail, in order to avoid unnecessary development of resistance.

Figure 4: Antibiotic advertising

Now on All Provincial Formularies Except Alberta*

Biaxin XL Is on Their Side

Patient To-do List
Take Biaxin XL Once Daily**

Biaxin XL To-do List

- Provide Clarithromycin Strength**
- Consider Resistance (documented low resistance with H. influenzae 1.6%, M. catarrhalis 0%, S. pneumoniae 7.8%)**
- Encourage Compliance with Once-daily Dosing**

ONCE-DAILY BIAXIN XL
CLARITHROMYCIN EXTENDED-RELEASE TABLETS
THE STRENGTH OF CONVENIENCE

*Biaxin XL (clarithromycin) is indicated in the treatment of mild-to-moderate infections caused by susceptible strains of the designated microorganisms in the following diseases: Community-acquired pneumoniae due to H. influenzae, H. parainfluenzae, M. catarrhalis, S. pneumoniae, C. pneumoniae (T401), or M. pneumoniae; 7-day treatment. Acute maxillary sinusitis due to H. influenzae, M. catarrhalis, or S. pneumoniae; 14-day treatment. Acute bacterial exacerbation of chronic bronchitis due to H. parainfluenzae, H. influenzae, M. catarrhalis, S. aureus, or S. pneumoniae; 7-day treatment. The efficacy and safety of Biaxin XL in treating other infections for which Biaxin RB and Pediatric Biaxin are approved have not been established.

**Most frequently reported adverse events were diarrhea (6%), abnormal taste (7%), and nausea (6%). Most of these events were described as mild or moderate in severity. Clarithromycin is contraindicated as concurrent therapy with zidovudine, zalcitabine, zalcitabine, or zalcitabine.

†Pediatric Biaxin is indicated for the treatment of acute otitis media caused by H. influenzae, M. catarrhalis, or S. pneumoniae. Most commonly reported adverse events in the digestive system were diarrhea (7%), vomiting (7%), abdominal pain (5%), dyspepsia (5%) and nausea (1%). Product Monograph available upon request.

Restrictions may exist by province (i.e., U.S., N.S., P.I., Sask.). Please write to your formulary for details.
Biaxin XL is presented as 2 x 500 mg tablets once daily (1000 mg q.d.) with food by the full course of treatment. Administration of Biaxin XL under fasting conditions is associated with approximately 70% lower AUC relative to administration with food. Biaxin XL must be taken with food to maximize bioavailability.
*Unique patient outcomes were collected in 25 medical centres in 9 provinces from October 1997 to June 2002: 7,564 in H. influenzae, 2,314 in M. catarrhalis and 1,991 in S. pneumoniae. Clinical significance has not been established.

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1-800-368-7462

Abbott Laboratories Limited
Biaxin XL, Biaxin, and Biaxin XL are trademarks of Abbott Laboratories.

(Advertisement from the Canadian Medical Association Journal, 13 September 2005.)

This advertisement for clarithromycin (Biaxin) suggests putting the medicine “at the top of your list” to treat children. Many common childhood infections do not require antibiotics.

Box 4: How to evaluate the text in pharmaceutical advertisements

- Are generic names used as frequently as brand names and is the type the same size as that used for the brand name?
- Are claims in advertisements restricted to unambiguous clinical outcomes or meaningful economic claims?
- If there are claims about surrogate endpoints is there also information that directly links changes in these end points to meaningful clinical outcomes?
- Are all claims for safety, effectiveness and cost-effectiveness in advertisements backed up by high-quality evidence (evidence from meta-analyses or randomised, controlled trials)?
- If there are claims for use of a medicine in a particular population are they based on high-quality evidence that comes from medicine use in that population?
- Is information about safety given the same prominence and placement as information about effectiveness?
- Do economic claims give actual prices of different alternatives? Are there vague claims about costs, such as “costs less”?
- Do advertisements for antibiotics recommend use that is consistent with guidelines to prevent unnecessary development of resistance?

Pictures and images in advertisements

Pictures and images in journal advertisements can help shape the way that doctors view patients. Some common portrayals are: as helpless victims of disease, as partners in developing therapeutic options, as people who are demanding, as being intelligent or emotional. The images in advertising can also sway how physicians and pharmacists view themselves, for example, as caring professionals able to solve a patient’s problem.

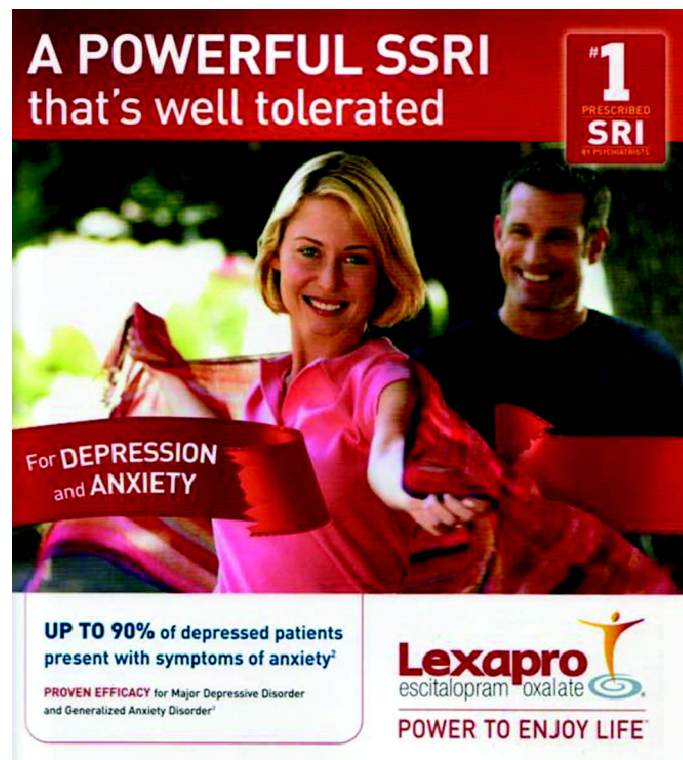
These pictures can either reinforce or challenge generally held societal prejudices about different groups of people. Pictures and images can also serve as metaphors as advertisers seek to identify their products with a particular image, e.g., a maker of an antidepressant may hope to identify its medicine with images of brightness as a symbol of recovery. The use of metaphors tends to reduce illness to a single dimension and treatment to a single modality (medicines) thereby taking illness out of its social context and simultaneously denying a role for any other form of therapy.

• Reinforcement of social stereotypes

Much of the analysis of the way different groups are portrayed in advertising has focused on women. A random sample of US general and specialty medical journals found that men were usually depicted as doctors and women as patients taking medicines. In general, men were more often portrayed as workers and when women were shown working, it was usually in stereotypically feminine jobs such as secretaries and waitresses (Hawkins, 1993).

An analysis of advertisements for antidepressants in Scandinavian and US journals in 1995 showed that the Scandinavian advertisements tended to construct antidepressants as female gendered and depression as detached from any social context. Both US and Swedish advertisements used images of couples and showed the medicine as being key to maintaining the relationship, and the woman as the person needing the medicine (Lovdahl, 1999).

Figure 5: Images of women in antidepressant advertising



(Advertisement from the American Journal of Psychiatry 2006;163(9)).

The image in this advertisement suggests a number of things about depression, women and pharmaceutical treatments.

Although depression is diagnosed about twice as often in women than in men the ratio of females to males in advertisements in the *American Journal of Psychiatry* was 5:1 and in *American Family Physician* it was 10:0. The authors of this study speculated that the overrepresentation

of women may reinforce cultural stereotypes and result in diagnosis and treatment of women in gender-biased ways (Hansen, 1995). Another analysis noted that women were under-represented in advertisements for cardiovascular medications and that this could contribute to under-diagnosis of cardiovascular disease in women, together with factors such as differences in symptoms and expression of disease (Ahmed, 2004; Leppard, 1993).

There are also biases in the way that the elderly are presented in journal advertisements. In a sample of advertisements from Canadian medical journals, Lexchin (1990) found that the special needs of the elderly often did not appear to be taken into account and this could contribute to misprescribing to the elderly. Finally, in multicultural societies, advertisements have a preponderance of whites both as health-care providers and as patients (Hawkins, 1993; Munce, 2004).

• Appeals to myth

The use of images to construct mythical and potentially misleading associations between disease and medicine was evaluated in 26 advertisements appearing in issues of the *British Medical Journal* between 1999-2001 (Scott, 2004). This analysis suggests “*that myth is often deployed in drug advertising to depict exaggerated therapeutic efficacy: armed with such drugs, the clinician can liberate patients from the oppression of disease and restore them to normality. With medicine as their alibi advertisers exploit the nude.... Mythology transports the clinician into a wider sociocultural context than that of medicine alone. Viewing exotic or erotic scenes derived from ‘old masters,’ the reader is relocated from office to gallery, obtaining visual relief from the clinical grind.... Associations between diseases and drugs are made to seem natural, unmotivated by commercial interest.*”

Ferner and Scott (1994) note that symbols in advertisements have complex and multiple meanings and are able to evoke strong feelings. Doctors may be unaware of the hidden messages in images or may be reluctant to acknowledge them and this reluctance may leave them vulnerable to misprescribing.

Psychotropic medicine advertisements are particularly prone to using symbols or metaphors to convey hidden meanings. Kleinman and Cohen (1991) showed how images in advertisements distort debate over treatment options and legitimise existing social relations and attitudes. The majority of advertisements in the *British Journal of Psychiatry* and its Irish counterpart used metaphors as their main marketing strategy instead of providing adequate information necessary for appropriate prescribing (Quinn, 1997). Finally, an analysis of eight advertisements for antidepressants appearing in issues of the *Canadian Journal of Psychiatry* between 1989 and 2002 showed “*how existing paradigms of social worth can be used by the drug industry to create perceptions of their products, with the intention of promoting sales.*” (Peppin, 2003).

Box 5: How to evaluate pictures and images in pharmaceutical advertisements

- Do the people portrayed in the advertisements reflect the racial and ethnic composition of people in your country?
- Are both men and women portrayed in advertisements as both patients and health-care providers in equal numbers?
- Are the ways that men and women are portrayed (as workers, facial expressions, body language, etc.) similar?
- How are the elderly portrayed in advertisements?
- Are symbols or metaphors used in advertisements?
- What kinds of associations do these symbols and metaphors convey?
- Are illnesses portrayed as individual events or are they put into a social context?

Conclusion

As a minimum, advertisements for prescription medicines should contain the key information listed in the WHO Ethical Criteria concerning the medicine name and manufacturer, who it is indicated for, key beneficial and harmful effects and reference to scientific evidence to back treatment claims. This provides basic knowledge of a medicine's characteristics required for prescribing decisions. However, the presence of this information does not ensure that the advertisement promotes appropriate use. To critically appraise advertisements, it is important to systematically look at all of the advertisement's elements: data and graphs, text, references and images. Often social as well as medical dimensions come in, such as the portrayal of the relationship between doctors and patients, or the way women or the elderly are portrayed. Additionally, myth and emotive imagery may be used to create an impression of a brand that has little to do with evidence of the product's effects and characteristics. Underlying any critical appraisal of advertising, the key question is what the messages and images in the advertisement mean for patient health.

Student exercises

1. Advertising analysis

- Look at the advertisement shown in Figure 1 in this chapter. Compare the information provided to the types of information that should be present, according to the WHO Ethical Criteria (Box 1). What information is missing? Next to each type of missing information, explain whether you think it is needed and why or why not.
- Pick three or four advertisements from current issues of the major medical or pharmacy journal(s) in your country and examine and compare them to reliable and unbiased sources of information about the medicine to determine if they contain the information recommended in the WHO Ethical Criteria. (See Chapter 8 for more details on sources of reliable and unbiased information.)
- Find a local advertisement that includes at least one graph. Use the criteria given in Box 2 in this chapter to evaluate the content.
- Collect the advertisements in the latest issue of your national medical or pharmacy journal. How many advertisements include references? How many are to “data on file”, to poster presentations, or to review articles? How many citations are incomplete? How often did companies sponsor the studies? Try to retrieve all of the references from one advertisement. Did you succeed? Why or why not? Using the section in Chapter 8 on critical appraisal, comment on the strength of methodology and relevance to claims for which they were cited.
- Analyse the different components of the advertisements (graphs and data presentation, text, references and pictures/images) according to the criteria outlined in this chapter.
- See the list of independent information sources in Chapter 8. Try to find a reference covering at least one of the medicines for which you have an advertisement. How does this information compare with the messages in the advertisement?
- Choose a convenience sample of health-care professionals, such as your professors, friends or colleagues. Show the current advertisements to them and ask them their opinions of the advertisements. Do their opinions match your analysis? What differences are there and how do you think those differences would affect prescribing?

2. Create your own spoof advertisement

- Choose a medicine that is currently being heavily advertised and for which you also have a source of independent information (see Chapter 8 for references).

- Pick a recent advertisement for the medicine.
- Go through the advertisement and pick out any implied or stated messages in images, text or graphs and data that are inconsistent with the independent information.
- Look as well for any social messages or use of myths in the advertisement.
- Create your own spoof advertisement for this medicine using similar messages. This can be in any form: a journal advertisement, a poster, a promotional patient brochure, a song to play on radio, a short play, a video and so on.

3. Debate the role of advertising in medical journals

- Some critics of pharmaceutical advertising say that health professional journals should not accept any advertisements from pharmaceutical or medical device companies. (See: Fugh-Berman A, Alladin K, Chow J (2006). *PLoS Medicine* 3 (6):e130. (See: <http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0030130>).
- Others cite freedom of expression and say that pharmaceutical companies should be able to advertise as long as the advertisements are not deceptive.
- Divide into teams and debate the pros and cons of health professional journal policies banning pharmaceutical advertising entirely versus continuing to run the advertisements but regulating them more strictly.

4. Types of advertising claims

- Collect 6 advertisements from a medical or pharmacy journal.
- Make a list of all the claims in the text and headlines for each of the advertisements.
- How many of them fit into each category listed in Table 2?

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Doctors and pharmacists play a key role in ensuring the rational use of medicines. As gatekeepers to care, they need to assess different treatment options, including pharmacotherapy, and consider each for potential benefit and harm. However, in recent years, growing concern has focussed attention on the relationship between health-care professionals and the pharmaceutical industry - particularly the industry's influence on prescribing and dispensing decisions using a range of promotional tools, which can influence rational treatment choices.

In 2005, a World Health Organization (WHO)/Health Action International (HAI) cross-sectional, international survey of educational initiatives on pharmaceutical promotion found that whilst many schools and colleges included this topic in their curriculum, most spent less than one day on it. The survey showed that although medical and pharmacy educators recognise the need for education on pharmaceutical promotion and sometimes do their best to incorporate it into their work, it is mostly limited.

This draft manual is a first step in addressing the need for medical and pharmacy professionals to reconsider their central role as a target for pharmaceutical marketing. Its nine chapters explore a spectrum of related topics, providing a resource for curriculum development that will help tomorrow's doctors and pharmacists be better prepared to face the promotional activity to which they will be exposed. In addition, it emphasises the importance of analysing information about medicines so that health professionals can make rational choices that will contribute to the health of patients.