

What information do physicians receive from pharmaceutical representatives?

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ABSTRACT

OBJECTIVE To assess the information pharmaceutical sales representatives provide to physicians.

DATA SOURCES A MEDLINE search from January 1966 to May 1996 was done using combinations of the terms pharmaceutical industry, drug information services, drug utilization, physician's practice patterns and prescriptions, and drugs. Studies identified from this search were supplemented by material from my personal library.

STUDY SELECTION Studies had to be conducted in industrialized countries, based on direct observations of actual physician and sales representative contacts, and reporting quantitative results on the quality of information transmitted.

SYNTHESIS Four studies were included. Representatives usually mentioned the indications for their drugs, but omitted safety information. Representatives' information frequently contained inaccuracies.

CONCLUSION Sales representatives present only selected, usually positive, information about their products. Canadian doctors should not be passive recipients of information provided by sales representatives. Physicians who choose to continue to see representatives must critically compare the information they get from them with that contained in scientific publications.

RÉSUMÉ

OBJECTIF Évaluer la qualité de l'information dispensée aux médecins par les représentants commerciaux de l'industrie pharmaceutique.

SOURCE DES DONNÉES Recherche dans MEDLINE couvrant la période de janvier 1966 à mai 1996 en utilisant les mots clés « pharmaceutical industry, drug information services, drug utilization, physician's practice patterns and prescription » et « drugs ». Cette recension des études a été complétée avec du matériel provenant de ma bibliothèque personnelle.

SÉLECTION DES ÉTUDES Les études devaient être menées dans un pays industrialisé, basées sur des observations directes de contacts entre des médecins et des représentants commerciaux et présenter des résultats quantitatifs portant sur la qualité de l'information transmise.

SYNTHÈSE Quatre études furent sélectionnées. Les représentants mentionnaient habituellement les indications des médicaments mais omettaient l'information concernant l'innocuité. Les renseignements dispensés par les représentants étaient souvent inexacts.

CONCLUSION Les représentants commerciaux se limitent à présenter une information présélectionnée, habituellement positive, concernant leurs produits. Les médecins canadiens ne devraient pas se limiter à recevoir passivement l'information dispensée par les représentants commerciaux. Les médecins qui font le choix de continuer à recevoir les représentants doivent procéder à une comparaison critique de l'information reçue à celle contenue dans les publications scientifiques.

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What information do physicians receive from pharmaceutical representatives?

Most doctors (85% to 90%) in Canada see pharmaceutical sales representatives (detailers)^{1,2} about once every second week; sales representatives are family physicians' second most frequently used source of drug information.³ Ample evidence in the literature shows that detailers are effective in changing physicians' prescribing behaviour. At one institution, 25% of internal medicine faculty and 32% of residents reported that they had changed their practice at least once in the preceding year because of a discussion with a sales representative.⁴ Almost 50% of Canadian psychiatric housestaff thought that discussions with sales representatives affected their prescribing behaviour.⁵

The more contact Australian doctors had with detailers, the more quickly they began using temazepam and the more rapidly it became their hypnotic drug of choice.⁶ Physicians who requested formulary additions were much more likely to have seen sales representatives from the companies making the drugs in question than were other doctors in the same hospital.⁷

Because detailers are so influential and so widely used, the information they provide to doctors must be both accurate and complete. Speaking at a 1994 Food and Drug Law Institute meeting Lucy Rose, director of the Food and Drug Administration's Drug Marketing Division, noted that sales representatives were being provided with excessive information about unapproved indications for drugs and that some companies were setting sales goals far higher than the total patient population for which products were approved.⁸

In Canada the activities of sales representatives are governed by the Pharmaceutical Manufacturers Association of Canada's (PMAC) Code of Marketing Practices. This code requires detailers to "provide full and factual information on products, without misrepresentation or exaggeration. Representatives' statements must be accurate and complete and must not be misleading, either directly or by implication."⁹

From time to time anecdotal reports have suggested that Canadian sales representatives are supplying incorrect information,^{10,11} but since PMAC has no program for actively monitoring detailers' interactions with physicians, it is unclear whether these reports are just isolated events or widespread practice. This review assesses, in a systematic manner, the information sales representatives provide to physicians.

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Materials and methods

A MEDLINE search from January 1966 to May 1996 was done using combinations of the terms pharmaceutical industry, drug information services, drug utilization, physician's practice patterns and prescriptions, and drugs. References in articles retrieved from this search were scanned and possibly relevant material obtained. This literature was supplemented by material from my personal library. To be included in this review, studies had to meet the following criteria: be conducted in industrialized countries (operationally defined as countries that are members of the Organization for Economic Cooperation and Development), be based on direct observations of actual physician and sales representative interactions, and report quantitative results about the information that sales representatives transmitted.

The following information was extracted from each eligible study: study characteristics (setting, sample, design, number of details observed, and total number of drugs being detailed); information transmitted and the accuracy of that information as judged by the study authors (number of times that indications, safety information, generic name, and price were mentioned, percentage of statements made during the detail that were inaccurate, percentage of interactions containing an incorrect statement). Data extraction and synthesis were done solely by me.

Results

Three journal articles were identified by the MEDLINE search: two on trials conducted in Finland in 1975¹² and 1986¹³ and one on a trial in the United States in 1993.¹⁴ Also included was a study of Australian doctors conducted from December 1992 to February 1994 as part of a master's degree thesis.¹⁵

Characteristics of the studies are reported in **Table 1.**¹²⁻¹⁵ In the Australian study, detailers made one-on-one presentations to doctors in their offices. In the Finnish and American studies, sales representatives gave presentations to groups of medical students, residents, and doctors in either hospitals or outpatient clinics. In the Finnish studies, observers filled out questionnaires after the interaction, while in the American and Australian studies interactions were tape recorded and transcribed. The total number of details observed ranged from 13 to 69. During each detail two to three drugs were discussed.

Table 2¹²⁻¹⁵ summarizes the main points from these surveys. While representatives usually mentioned the indications for their drugs, they did not bring up prices, side effects, or contraindications

Table 1. Characteristics of studies examining information transmitted by detailers

| STUDY CHARACTERISTICS | FINLAND 1975 ¹² | FINLAND 1986 ¹³ | UNITED STATES 1993 ¹⁴ | AUSTRALIA 1992-1994 ¹⁵ |
|-----------------------|---|---|--|--|
| Setting | Hospital or outpatient clinic | Hospital or outpatient clinic | Noontime hospital teaching conferences | Doctors' offices |
| Sample | Medical students and graduate doctors | Medical students and graduate doctors | Medical students and residents | General practitioners |
| Design | Questionnaire completed by observer after interaction | Questionnaire completed by observer after interaction | Audiotape of interaction and transcription | Audiotape of interaction and transcription |
| No. of interactions | 46 | 69 | 13 | 16 |
| No. of drugs detailed | 115 | 173 | — | 33 |

spontaneously. Generic names were mentioned in about 50% to 75% of interactions.

In the American study, all 106 statements made by detailers were evaluated against three criteria: consistency with information in the 1993 *Physicians' Desk Reference*¹⁶; consistency with the opinion of a pharmacist and a physician-clinical pharmacologist; and consistency with information retrieved from reference books, drug company brochures, and MEDLINE from 1985 to 1993. Twelve statements (11%) failed to meet any of these criteria and were, therefore, judged inaccurate. All these inaccurate statements made the drug discussed appear better than it actually was. Not one of the false statements made during the presentation was challenged and, when residents were subsequently questioned, only 26% recalled hearing a detailer make an inaccurate claim.

The Australian study compared information in the detail with information in that country's version of the product monograph. For eight drugs there were inaccuracies in the dosage and administration and for five in the indications. Australia has a set of widely accepted guidelines covering various classes of drugs. These guidelines were applicable to 21 of the 33 products being detailed but were not referred to in any case.¹⁵

The studies reported that, when competitors' products were mentioned, almost invariably it was in an unfavourable context.¹²⁻¹⁵ Similarly, all four studies concluded that, when information on safety was given, it was usually done in a way that cast the representative's product in a favourable light.¹²⁻¹⁵

Discussion

Four surveys on the quality of the information sales representatives provide to doctors were undertaken in three industrialized countries from 1975 to 1994. In

general, the results were consistent across time and country: sales representatives almost always mentioned the indication(s) for the drug that they were detailing and frequently gave the generic name. On the other hand, they failed to give out safety information and, when safety information was mentioned, it was often done to cast the drug being detailed in a favourable light. There were frequently inaccuracies in the information representatives transmitted.

Limitations

There are limitations in the studies that form the basis for this review and in the review itself. For this study, it is possible that proprietary information exists that was not located by the search methods employed. All of the studies reported used convenience samples of physicians and, therefore, might not be representative of all contacts. The studies that relied on physicians' recall of the interaction^{12,13} have the obvious limitation inherent in any method that relies on memory, although the fact that the questionnaires were filled out right after the interaction took place probably means that little information was lost. In the Australian study, the physician being detailed did the recording so some aspects of the interaction might not have been recorded.¹⁵

Other limitations in the studies could make the interactions look better or worse than they actually were. For instance, the group interactions reported by Hemminki^{12,13} and Ziegler et al¹⁴ might not have been reported as accurately as the one-on-one interactions. Audiotaping cannot assess use of visual aids, printed materials, and samples. Ziegler et al¹⁴ did not discuss areas of omission in the presentations that they recorded. Roughead¹⁵ did not compare claims made by representatives against the medical literature, nor

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What information do physicians receive from pharmaceutical representatives?**Table 2. Information provided by detailers**

| INFORMATION | FINLAND 1975 ¹² (N=69) % | FINLAND 1986 ¹³ (N=46) % | UNITED STATES 1993 ¹⁴ (N=13*) % | AUSTRALIA 1992-1994 ¹⁵ (N=33†) % |
|---|--|--|---|--|
| Item spontaneously brought up by detailer | | | | |
| • Indications | 91 | 90 | | 73 |
| • Generic name | 78 | 62 | | 45 |
| • Price | 35 | 29 | | 12 |
| • Side effects | 29 | 27 | | 27 |
| • Contraindications | 27 | 25 | | 0 |
| Incorrect statements | | | 11 | |
| Details containing an inaccuracy | | | 62 | 39 |

*Number of interactions.
†Number of drugs detailed.

did she classify or rate information in terms of seriousness of omissions and danger of inaccuracies.

The kind of information representatives provide is probably the reason that research from Belgium,¹⁷ the United Kingdom,¹⁸ and the United States^{19,22} has consistently shown an association between using information provided by detailers and prescribing inappropriately. The more frequently physicians saw detailers, the more prone they were to use pharmacotherapy rather than nondrug therapy even where nondrug therapy was the best option,¹⁷ the more often they favoured commercial views about the use of a product rather than views promoted in the scientific literature,¹⁸ the more likely they were to prescribe antibiotics inappropriately,¹⁹ the less likely they were to prescribe generic drugs,²⁰ and the more likely they were to use more expensive medications when equally effective but less costly ones were available.^{21,22} While direct evidence on the situation in Canada is lacking, interactions quite likely follow the pattern described above, both in terms of the quality of the information and the effect on prescribing.

Canadian physicians could choose not to see representatives, but few doctors have made that choice. Those who continue to see representatives must understand that doctors cannot afford to be passive players in the interaction, content to just accept the information provided by representatives. We have to be aware of our own needs, set the agenda when we see representatives, and demand objective information from them in the form of either peer-reviewed randomized, controlled trials or meta-analyses. We also need to be sure that we are getting an accurate picture of the relative worth of the product being detailed. This can be accomplished by ensuring that we receive a balanced view of the risks

and benefits of the drug and by comparing the representative's information with information in sources such as *The Medical Letter*, *Therapeutic Choices*,²³ and *Drugs of Choice: a formulary for general practice*.²⁴

Conclusion

Four studies over 20 years have consistently demonstrated that detailers selectively transmit only positive information about their companies' products. Side effects and contraindications are rarely mentioned, and the information that detailers give to physicians is frequently inaccurate. Taking information at face value will not serve the best interests of our patients. We need to press the pharmaceutical industry to mount an active campaign to monitor and improve the quality of representatives' presentations. ♦

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THERAPEUTIC INFORMATION



NAME OF DRUG

ZYRTEC (cetirizine hydrochloride) 10 mg Tablets **THERAPEUTIC CLASSIFICATION.** Histamine H₁ Receptor Antagonist. **MODE OF ACTION.** ZYRTEC (cetirizine hydrochloride), a human metabolite of hydroxyzine, is a histamine H₁ receptor antagonist anti-allergic compound; its principal effects are mediated via selective inhibition of peripheral H₁ receptors. ZYRTEC (cetirizine hydrochloride) is distinguished from other histamine H₁ receptor antagonists by the presence of a carboxylic acid function. This difference may be partly responsible for the selectivity of ZYRTEC (cetirizine hydrochloride) seen in pharmacologic models and its distinctive pharmacokinetic properties in humans. **INDICATIONS AND CLINICAL USE.** ZYRTEC (cetirizine hydrochloride) is indicated for the relief of symptoms associated with seasonal allergic rhinitis, perennial allergic rhinitis and chronic idiopathic urticaria; i.e. sneezing, rhinorrhea, post nasal discharge, tearing and redness of the eyes, pruritis and hives. **CONTRAINDICATIONS.** ZYRTEC (cetirizine hydrochloride) is contraindicated in those patients with a known hypersensitivity to it or to its parent compound, hydroxyzine. **WARNING.** Pregnancy: No teratogenic effects were caused by oral doses as high as 60, 188 and 133 times the maximum clinically studied human dose in mice, rats and rabbits, respectively. No effects on reproduction and fertility were observed at doses as high as 40 and 10 times the maximum recommended human dose in male and female mice, respectively. An oral dose 60 times the maximum clinically studied human dose in female mice did not affect parturition or lactation. Although the animal studies are not indicative of any adverse effects during pregnancy at clinically relevant doses, such studies are not always predictive of a human response. There are no adequate and well controlled studies in pregnant women. Until such data become available, ZYRTEC (cetirizine hydrochloride) should not be used during pregnancy, unless advised otherwise by a physician. Nursing Mothers: Studies in beagle dogs indicate that approximately 3% of the dose is excreted in milk. The extent of excretion in human milk is unknown. Use of ZYRTEC in nursing mothers is not recommended, unless directed otherwise by a physician. Pediatric Use: Unless directed otherwise by a physician, ZYRTEC should not be administered to children below 12 years of age since its safety and effectiveness in this age group has not yet been established. Activities Requiring Mental Alertness: Studies using objective measurements have shown no effect of ZYRTEC (cetirizine hydrochloride) on cognitive function, motor performance or sleep latency. However, in clinical trials the appearance of some CNS effects, particularly somnolence,

have been observed. Due caution should be exercised when driving a car or operating potentially dangerous machinery. Use in the Elderly: ZYRTEC (cetirizine hydrochloride) was well tolerated by patients aged 65 and over. In patients whose creatinine clearance is reduced, a starting dose of 5 mg/day is recommended (see Human Pharmacokinetics in Product Monograph). Occasional instances of liver function test (transaminase) elevations have occurred during ZYRTEC (cetirizine hydrochloride) therapy. This incidence was 1.6% in the short-time trials and 4.4% in the 6 month trials. These liver enzyme elevations, mainly SGPT, were generally reversible. There was no evidence of jaundice or hepatitis, and the clinical significance is presently unknown. ZYRTEC should be used with caution in patients with pre-existing liver disease. In patients with moderate hepatic impairment, a starting dose of 5 mg is recommended. Use in Asthmatics: ZYRTEC has been safely administered to patients with mild to moderate asthma. ZYRTEC did not cause exacerbation of asthma symptoms. **Drug Interactions:** No clinically significant drug interactions have been found with theophylline, pseudoephedrine, cimetidine, erythromycin and ketoconazole. Epidemiologic data suggests that there also would not be interaction with other macrolide antibiotics or imidazole antifungals. In clinical trials, ZYRTEC (cetirizine hydrochloride) has been safely administered with beta-agonists, non-steroidal anti-inflammatory drugs, oral contraceptives, narcotic analgesics, corticosteroids, H₂-antagonists, cephalosporins, penicillins, thyroid hormones and thiazide diuretics. Interaction studies with ZYRTEC and alcohol or diazepam indicate that ZYRTEC does not increase alcohol-induced or diazepam-induced impairment of motor and mental performance. **SIGNIFICANT ADVERSE EFFECTS.** In clinical development programs (domestic and international), ZYRTEC (cetirizine hydrochloride) has been evaluated in more than 6000 treated patients at daily doses ranging from 5 to 20 mg. The most common adverse reactions were headache and somnolence. The incidence of headache associated with ZYRTEC (cetirizine hydrochloride) was not different from placebo. The incidence of somnolence associated with ZYRTEC was dose related and predominantly mild to moderate. The incidence of somnolence in fixed dose studies was 6% for placebo, 11% at 5 mg and 13.7% at 10 mg. Dry mouth was reported by 5% of patients (versus 2.3% for placebo). Fatigue was reported by 5.9% of patients (versus 2.6% for placebo). Most adverse reactions reported during ZYRTEC (cetirizine hydrochloride) therapy were mild to moderate. The incidence of discontinuation due to adverse reactions in patients receiving ZYRTEC was not significantly different from placebo (1.0% vs 0.6%, respectively, in placebo-controlled trials). There was no difference by gender or by body weight with regard to the incidence of adverse reactions. Occasional instances of transient, reversible hepatic transaminase elevations have occurred during ZYRTEC therapy, without evidence of jaundice, hepatitis or other clinical findings. Adverse events which were reported at an incidence of greater than 1/100 in clinical trials are listed in Table 1. Table 1 Adverse Reactions Reported in Placebo Controlled United States Zyrtec trials (Maximum Dose of 10 mg) at Rates of 1% Greater (Percent Incidence).

TABLE 1

| ADVERSE EXPERIENCE | ZYRTEC (N = 2034) | PLACEBO (N = 1612) | DIFFERENCE OF PERCENTAGE |
|--------------------|-------------------|--------------------|--------------------------|
| Headache | 17.6 % | 17.9 % | (0.3)* |
| Somnolence | 13.7 | 6.3 | 7.4 |
| Fatigue | 5.9 | 2.6 | 3.3 |
| Dry mouth | 5.0 | 2.3 | 2.7 |
| Nausea | 2.5 | 2.9 | (0.4)* |
| Pharyngitis | 2.0 | 1.9 | 0.1 |
| Dizziness | 2.0 | 1.2 | 0.8 |
| Insomnia | 1.4 | 1.2 | 0.2 |
| Epistaxis | 1.2 | 0.6 | 0.6 |
| Coughing | 1.0 | 0.6 | 0.4 |
| Abdominal Pain | 1.0 | 0.9 | 0.1 |
| Dyspepsia | 0.8 | 1.6 | (0.8)* |
| Pruritis | 0.3 | 1.2 | (0.9)* |

(* = higher frequency in placebo group.)

DOSAGE AND ADMINISTRATION. Adults and adolescents 12 and over: The recommended initial dose of ZYRTEC (cetirizine hydrochloride) is 5 to 10 mg, depending on symptom severity, given as a single daily dose, with or without food. Most patients begin with a dose of 10 mg. The time of administration may be varied to suit individual patient needs. Clinical studies to date support treatment for up to 6 months thus medical recommendation is advised for long-term use. Elderly: In patients with moderate hepatic and/or renal impairment, a starting dose of 5 mg/day is recommended. **Stability and Storage Recommendations:** Store at room temperature between 15-30°C. Availability: Film-coated scored Tablet: 10 mg of cetirizine hydrochloride. For commercial use, tablet packaging: plastic bottles of 100 and 500 and blister packages of 18. *Product monograph is available on request.*

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