PHARMACOEPIDEMIOLOGY AND DRUG SAFETY **9**: 207–214 (2000)

ORIGINAL REPORT

Surveillance of a Recently Switched Non-prescription Medicine (Diclofenac) Using a Pharmacy-based Approach

NATALIE J. GAULD MPharm, MPS[1], JOHN P. SHAW PhD,MPS[2]*, LYNNE M. EMMERTON PhD, MPS[1] AND B. DAMIAN PETHICA MD, MRCGP[3]

[1] *School of Pharmacy, University of Otago, Dunedin, New Zealand*

[2] *Faculty of Medicine and Health Science, The University of Auckland, Auckland, New Zealand*

[3] *Novartis New Zealand Ltd. (formerly Ciba-Geigy New Zealand Ltd.), Auckland, New Zealand*

SUMMARY

Purpose — Postmarketing surveillance of prescription medicines is a routine practice, yet similar evaluation of non-prescription medicines, including those recently switched from prescription status, is uncommon. This study presents the methodologic issues and limitations of the use of pharmacies in the 'post-reclassification' surveillance of oral diclofenac potassium 25 mg which had been recently switched from physician prescription to non-prescription sale.

Methods — Consenting user-purchasers were recruited from 175 New Zealand pharmacies over 4 months. Purchasers were mailed a questionnaire for completion 7 days post-purchase. Those purchasers who met criteria for being potentially 'at risk' of adverse events were re-surveyed 30 days post-purchase. A descriptive analysis was carried out using *t*-test and chi-square as appropriate. These results were compared to those from other types of studies in this area.

Results — The 1240 recruited purchasers returned 990 valid questionnaires (80% response). Of these 557 (56%) met 'at risk' criteria and received the second questionnaire with 480 valid returns (86.2% response).

Conclusions — Useful data was gathered on the 'real-life' usage of a medicine recently reclassified from prescription to non-prescription sale. The use of community pharmacies as recruiting centres was found to be effective.

KEY WORDS — NSAID; reclassified medicines; diclofenac; non-prescription medicines; community pharmacies; postmarketing surveillance; New Zealand

COMMENTARY

With an increasing range of medicines being reclassified from prescription-only to over-the-counter availability, there is a need for more research on their safety and efficacy in the less controlled non-prescription environment. This pharmacy-based study, using pharmacists as recruiters and mail follow-up of purchasers, yielded useful data on the non-prescription use of a recently switched product, diclofenac. The advantages and limitations of this approach were compared to others in the literature. With some suggested improvements, the current method represents a useful means of collecting data concerning switched medicines that might not otherwise be available.

INTRODUCTION

There is a worldwide trend for the reclassification of prescription medicines to allow over-the-counter (OTC) purchase.[1–3] The main reasons why medi-

* Correspondence to: J. P. Shaw, School of Pharmacy, University of Otago, Dunedin, New Zealand.

Contract grant sponsor: Novartis New Zealand Ltd. (formerly Ciba-Geigy New Zealand Ltd.).

Received 9 June 1998
Accepted 10 December 1999

cines are 'switched' are consumer convenience and potential cost savings for governments and third-party payers.[4] In the non-prescription setting, there is less control over the use of such medicines and obvious potential for increased adverse events due to misuse and overuse.

To be considered as switch candidates, the agents concerned must have well-established efficacy profiles as prescription medicines. In addition, they must have favourable adverse events and drug interaction profiles, relatively low toxicity, and a low potential for abuse.[5] The information that supports such safety and efficacy is almost entirely derived from controlled clinical trials and post-marketing safety surveillance data.[6] Each of these approaches has limitations and may not always predict outcomes in a non-prescription setting.[7,8] A number of strategies for assessment of switched medicines have been suggested, including pharmacy-based clinical trials and surveillance studies, but these have been difficult to implement.[9,10]

Countries differ with regard to how non-prescription medicines may be sold. In the United States, the Food and Drug Administration (FDA) has determined that if the product is safe enough to be used in self-medication, and is adequately labelled, then further controls are unnecessary.[11] Elsewhere, there is a variety of approaches ranging from the restriction of all non-prescription medicines to pharmacy-only or pharmacist-only sale, to a mix of pharmacy-only and general retail availability. Proponents argue that restricted availability provides for some supervision of use, and that this is particularly important for recently switched products.[11] In addition, the contact between pharmacist and patient allows for collection of data that may be useful for research purposes.

A class of 'switched' drugs that has attracted particular interest is the oral non-steroidal anti-inflammatory drugs (NSAIDs). The potential hazards of these agents if used inappropriately in a prescription setting are well recognized, but there is limited data, on their OTC usage, especially with regard to their safety when used in the full anti-inflammatory doses that are now possible.[12–14]

In New Zealand, the sodium salt of diclofenac (a NSAID) has been available by prescription for over 20 years. In 1992, diclofenac potassium was reclassified from prescription status to the Pharmacist-Only Medicine category and marketed as 25 mg tablets in a pack size of 30 tablets. Pharmacist-Only Medicines require direct involvement of a pharmacist in the sale, including adequate consultation with the purchaser, record-keeping, and restrictions on storage and direct pharmacy promotion. Such medicines are advertised by the manufacturers to the public via the print and electronic media. This intermediate level of control is generally used for recently reclassified medicines as a transition to more widespread OTC availability.

The objectives of the current study were to describe the 'real-life' usage of a recently switched medicine, and to explore the feasibility of using community pharmacies as a means of data collection for 'post-reclassification' surveillance. The potential benefits of such an approach might include a greater level of recruitment and more accurate data, and comparison was made between this method and others found in the literature.

METHODS

After a pilot study in the Dunedin area of New Zealand,[15] approval to proceed with a nationwide study was obtained from all regional Ethics Committees. A written open invitation to participate was made to all 1072 community pharmacies in the country. This was followed by regional meetings at which the study methods were explained. Participation was at the discretion of individual pharmacies, as there are no 'chain' stores.

Pharmacists acted as recruiting agents, and were instructed to invite purchasers to participate only after a sale of OTC diclofenac had been completed. Purchasers were provided with written and verbal information, and could take this away with them before making a decision. Inclusion criteria were purchase of the product for own use and written, informed consent. Exclusion criteria were purchase on behalf of another person, if unable to read and/or understand the consent form, or if already recruited.

The signed consent form, which included basic details such as the purchaser's name, address and telephone number, was faxed to the study centre on the day of purchase. A questionnaire with 29 items was mailed to purchasers for self-completion at 7 days post-purchase. Reminder telephone calls were made to non-respondents at 12 days post-purchase, when they could elect for telephone administration.

If responses in the 7-day questionnaire met predefined criteria, a second 8-item questionnaire was sent to be completed 30 days post-purchase, with telephone follow-up 12 days after the due com-

pletion date. The criteria were: use for more than three consecutive days; exceeding the individual or daily recommended dose; repurchase prior to questionnaire completion; possible contraindications; report of side-effects attributed to OTC diclofenac; or concurrent use of another NSAID. These criteria were deliberately broad to identify all purchasers who might possibly be 'at risk' of adverse effects.

There were no incentives for purchasers to participate. Pharmacists were reimbursed NZ$10 (approximately US$5) per recruitment for the time spent on administration. Recruitment took place over a 4-month period (August to November 1994), at which time OTC diclofenac had been available through pharmacy for about 18 months.

Validation sub-studies were undertaken in two separate randomly-selected samples of 25 participating pharmacies each. One sub-study compared purchasers' recollections of questions asked at the time of purchase with records kept by the pharmacists. The other compared the number, age and gender or purchasers who gave consent to participate with those who were not recruited, and also recorded the reasons for non-recruitment, by means of a log of all diclofenac sales. In addition, feedback from participating pharmacists was sought on completion of the study. This included their views on the study duration, reimbursement, time commitment, and communication with the researchers.

Data was recorded on an Excel database and checked by all records being double entered. Descriptive statistical analysis and cross tabulations (chi square and *t*-tests) were performed using the Statistical Package for the Social Sciences, Version 6 (SPSS®).

RESULTS

In response to the initial letter of invitation, 243 of the 1072 pharmacies throughout New Zealand (23%) indicated their intention to act as recruiting agents. During the study period, 175 pharmacies actually recruited Cataflam purchasers (16% of pharmacies nationwide). The total number of purchasers recruited was 1240 (median of 5.0 recruitment per pharmacy over the study period; range 1 to 36). There were 1004 respondents for the 7-day questionnaire and 990 valid responses (79.8% response). Of these, 556 met criteria for 'at risk' purchasers and were sent the 30-day questionnaire, with 480 returns (86.4% response).

From the 25 pharmacies used to evaluate all OTC diclofenac sales, 213 purchasers were invited to participate in the study, of whom 86 were recruited and 74 returned questionnaires (approximately one in three purchasers). Ineligibility was the primary reason for non-recruitment, most commonly because purchase was made on behalf of another person. Of the 67 eligible purchasers not recruited, the majority declined because they were 'in a hurry'. In the sub-study comparing pharmacists' and respondents' perceptions, there were 49 recruitments and 45 questionnaire returns. In general, purchasers reported lower levels of information obtained or provided by the pharmacist.

The mean age of respondents to the 7-day questionnaire was 45 years (range 14 to 92 years) and 580 (59.5%) were female, which was not significantly different than the sample of all OTC diclofenac sales. Previous use of OTC diclofenac was indicated by 381 (38.5%) respondents with the remaining 609 (61.5%) being first-time users. Moderate or better relief of symptoms was recorded by 824 (83.2%) of all users.

Table 1 shows the conditions for which the product was purchased. In addition 197 respondents (19.9%) indicated that they had shared some or all of their purchased diclofenac with another person. The conditions for which the recipients used the product were similar to those shown in Table 1 but with a higher proportion of citations for migraine/headache and dysmenorrhoea.

The mean maximum daily dose of the product used was 90 mg (3.6 tablets; 95% CI: 20 mg to 160 mg). Thirty-two (3.2%) respondents exceeded the manufacturer's maximum recommended dose of 150 mg (i.e. using seven or more tablets) on one or more days. It was noted that younger purchasers (less than 40 years of age) were more likely to exceed the recommended daily maximum dose, generally for the acute treatment of sports injuries and dysmenorrhoea.

The manufacturers recommend that users should consult a doctor if the product is used for more than 3 days. Of the respondents 394 (39.8%) used the product for more than 3 days but half of these said they did not consult a doctor, and 203 (20.5%) were using the product intermittently at 1 week. Only three purchasers reported use of the product continuously for more than 3 weeks.

Self-reported side-effects were recorded by 130 (13.1%) respondents, mostly minor gastrointestinal tolerability and tiredness/lightheadedness (Table 2). Sixty-six respondents (6.7%) had a possible contraindication for purchase, although it should

Table 1 — Conditions for which OTC diclofenac was purchased

Condition for which purchased	Frequency of mentions*	Percentage of total mentions
Acute musculoskeletal pain or inflammation (e.g. strains, sprains, tendon, joint and muscle pain or inflammation)	498	43.5
Vertebral column conditions (e.g. neck and back problems, pinched nerve, sciatica)	385	33.6
Arthritis or 'rheumatism'	60	5.2
Migraine or headache	60	5.2
Dental and oral pain or inflammatory conditions	43	3.8
Gynaecological conditions (e.g. dysmenorrhoea)	21	1.8
Gout	21	1.8
Post-operative pain or inflammation	18	1.6
Chronic non-traumatic conditions (e.g. occupational overuse syndrome)	15	1.3
Ear, nose or throat inflammation (e.g. cold, influenza symptoms, sinusitis, mumps, glandular fever)	13	1.1
Miscellaneous (e.g. pleuritic pain, headache from glaucoma)	12	1.1
Total	1145	100

* Data from 974 (98.4%) respondents; 168 purchasers mentioned more than one condition.

Table 2 — Purchasers' reports of side-effects associated with OTC diclofenac

Type of side-effects reported	Number of mentions*	Percentage of total mentions
Gastrointestinal system (e.g. mild nausea, dyspepsia)	78	54.9
Central and peripheral nervous system (e.g. tiredness, lightheadedness)	42	29.7
Skin	3	2.1
Urogenital system	1	0.7
Hypersensitivity (e.g. slight shortness of breath)	8	5.6
Others	10	7.0
Total	142	100

* Data from 130 (13.1%) respondents; 11 purchasers mentioned more than one side-effect.

be noted that in the majority of gastrointestinal complaints what was reported was a previous diagnosis (Table 3). The concurrent use of medicines (both prescription and OTC) is shown in Table 4. A breakdown of concurrent analgesic use is presented in Table 5. There were 40 mentions of concurrent prescription or OTC NSAID use.

At the conclusion of the study, feedback on the survey methods was received from 157 of the 175 recruiting pharmacies (85% response). The median time for recruitment was estimated at 5 min (range 1 to 15 min), 145 (93.5%) pharmacists were satisfied with the reimbursement of NZ$10 per recruitment, and 112 (75%) felt that the 4-month recruitment period was appropriate.

DISCUSSION

The origin of this study was a need for more information on the usage patterns and complications of OTC medications, and about the effects of rescheduling medications from prescription to non-prescription status. The approach taken was to use community pharmacists as recruiting agents of diclofenac purchasers, with subsequent questionnaire follow-up from the study centre. Both advantages and limitations of this approach are considered in the context of other studies that have sought similar information.

A number of commentators have advocated the restriction of all recently switched products to

Table 3 — Possible contraindications reported by OTC diclofenac purchasers

Type of possible contraindication	Number of mentions*	Percentage of total mentions
Previous diagnosis of peptic ulcer	49	73.1
Previous allergic reaction to pain medication	15	22.4
Worsening of asthma with analgesics	3	4.5
Total	67	100

* Data from 66 (6.7%) respondents; one purchaser mentioned two possible contraindications.

Table 4 — Concurrent medications reported by OTC diclofenac purchasers

Type of concurrent medication	Number of mentions*	Percentage of total mentions
Analgesics other than OTC diclofenac	145	26.8
Endocrine/hormonal	119	22.0
Cardiovascular	99	18.3
Respiratory	59	10.9
Central nervous system	32	5.9
Anti-infective	26	4.8
Vitamin/mineral	21	3.9
Gastrointestinal	19	3.5
Other	21	3.9
Total	541	100

* Data from 393 (39.7%) respondents; 148 purchasers mentioned more than one concurrent medication.

Table 5 — Concurrent analgesic use reported by OTC diclofenac purchasers

Type of analgesic	Number of mentions*	Percentage of total mentions
Paracetamol alone or in combination	92	63.5
OTC oral NSAID or aspirin	24	16.5
Prescription oral NSAID	16	11.0
Topical NSAID	13	9.0
Total	145	100

* Data from 132 (13.3%) respondents; 13 purchasers mentioned more than one concurrent analgesic.

pharmacist-only supervision for a limited period, and community pharmacist involvement in adverse drug reaction reporting schemes.[6,7] The classification of OTC diclofenac as a Pharmacist-Only Medicine in New Zealand was useful in the context of this study as it ensured that there was interaction between the purchaser and the pharmacist, allowing the latter to explain the purpose of the study and invite participation. This 'intervention' by the pharmacist may have lent authority to the study, and was reflected in the excellent survey response rates. These response rates were achieved without any monetary or other incentive to the respondents. Interestingly, other pharmacy-based studies which did employ incentives, had lower response rates.[16–18]

A possible concern in a study of this nature is whether payment to the pharmacist could influence the number or demographics of the patients who are encouraged to use the medication, particularly as the direct input of a pharmacist was a legal requirement in this case. It is important to ensure

that the study is for genuine postmarketing surveillance purposes and not simply a marketing exercise. The payment for pharmacists (approximately US$5 per recruitment) was deliberately set at a level to compensate the pharmacist only for the lost 'opportunity cost' of engaging in normal professional activities and was not intended as an incentive or 'finder's fee'. This figure was arrived at by consultation with the pilot study pharmacists who spent on average about 10 min in administering each recruitment. Given the low payment and low recruitment rate over the study period, it seems unlikely that pharmacists recruited patients inappropriately.

A similar approach (recruitment by pharmacists and follow-up by questionnaire) has been attempted in several Australian studies where the usage of non-prescription salbutamol inhalers by asthma patients was investigated when the product attained non-prescription status. Recruitment rates were lower than the current study, but the authors were able to conclude that OTC purchase of salbutamol is associated with infrequent consultation with doctors and under-treatment of asthma.[16,17]

In Sweden, a similar approach using pharmacists as recruiters was employed to document purchasers' views on product usage and opinions about the reclassification of topical hydrocortisone.[19] Other pharmacy-based studies of reclassified medicines have focused on the safety and usage aspects of H_2-antagonists in Denmark,[10] and on transdermal nicotine in New Zealand.[20] Each of these studies reported high levels of recruitment, and yielded useful information on the 'real-life' usage of the products. In the Danish study, this 'post-reclassification surveillance' was a mandatory condition of the switch.

A pharmacy-based study in Germany monitored the utilization of NSAIDs by assessing pharmacy prescription records and follow-up pharmacy-based interviews for a sample of NSAID users. The authors observed that pharmacies can be considered to be an important source of drug exposure information, and that they were able to obtain data on both prescription and non-prescription use of NSAIDs with good cooperation from the study pharmacists.[21] In hindsight, it might have been useful in the present study to have used prescription users of diclofenac as a comparison group to detect differences in the prescription and OTC uses of the medicine.

Clinical trials of OTC medicines in community pharmacies is another possible approach to the assessment of switched agents. This has been attempted in the United Kingdom and Denmark with studies on hayfever medications, analgesics, and transdermal nicotine.[22–24] Clearly, issues such as randomization, blinding and assessment were challenging but addressed successfully. In the antihistamine study, for example, two matched products were blinded to both pharmacist and purchaser, with self-assessment of control and side-effects using a symptom-scoring sheet. The use of health diaries to monitor therapeutic outcomes following the sale of OTC medicines has also been attempted. In a United Kingdom study of patients purchasing OTC hyperacidity products, there was a limited response with only 22% of recruited purchasers returning completed diaries.[25] This response rate was far less than the current study which suggests that recruitees prefer a single or periodic questionnaire to a regular diary.

There were some limitations to the study. The 16% participation rate of pharmacies is low. This may be because the invitation was unsolicited and there was no prior history of this type of research in New Zealand. The study required a high level of commitment over several months and there were few incentives to participate other than contribution to research and a small financial compensation for recruitment. It is possible that pharmacists who participated were more professional and better motivated than those who did not. This selection bias may have been reflected in the purchasers' perceptions of the product, and would be interesting to explore in a future study. More active and targeted recruitment, and familiarity with the procedure by pharmacists, might improve the pharmacy uptake.

Another limitation was that the median number of recruitments over a 4-month period was about five per pharmacy. This was not entirely surprising as OTC diclofenac was a relatively new product and its status as a Pharmacist-Only Medicine required that it was kept out of public reach in the pharmacy. It does suggest that a large proportion of purchasers did not participate and again introduces the possibility of selection biases. These concerns were addressed in part by the sub-study of all sales which suggested that about one in three OTC diclofenac purchasers became a respondent. Recruitment issues could be addressed by keeping track of all purchases in the study by means of a log book.

The study relied on self-reporting so that detail about concurrent medical conditions and side-effects was limited. This introduces the possibility

of information and misclassification biases. These concerns could have been addressed by direct interview of a sample of purchasers, follow-up with their medical notes, or the use of a diary. The exclusion criteria may have affected the representation of certain groups in New Zealand, particularly the Maori and Pacific Island populations and those with a poor grasp of English. In addition, perhaps elderly or 'sicker' persons were excluded because they could not physically access the pharmacy. These exclusions certainly limit the generalizability of the findings and merit further investigation.

Despite these limitations, the study has yielded useful information on how a recently reclassified product is used in 'real life'. In the majority of cases, oral diclofenac appeared to be used safely and to good effect. It is of concern, however, that a small number of individuals with hypersensitivities or contraindications were able to access the product or were using other potentially harmful concurrent medications, even though no serious adverse consequences were reported. The need for constant vigilance by both pharmacists and medical practitioners in routinely assessing patients' concurrent medications, both prescription and OTC, is reinforced by the findings of the current study.[26] It is also worth reflecting on the fact that similar products are widely available in some other countries (for example, the United States) through general retail outlets with no health professional supervision.

Perhaps the use of a 'transition' class of drugs for recently reclassified products, allowing for supervised sale by pharmacists for a defined period after switching, has greater appeal as more potent agents become available OTC. An encouraging aspect of the current study was the support and goodwill of the participating pharmacists. They were well disposed to the study as evidenced by their views on the study materials, methods, level of reimbursement and timeframe. If the limitations of the current methods can be addressed, then this pharmacy-based approach may provide information not otherwise available on the safety and efficacy of OTC medicines. It may even be feasible to propose that regulatory authorities consider a formal 'post-reclassification' surveillance programme using similar methods for all newly reclassified products.

CONCLUSION

This pharmacy-based study of the usage of a recently reclassified medicine has illustrated the potential for further research of this nature through community pharmacy. Such research is important as the number and range of switched products continues to grow. The use of pharmacists as recruiting agents with survey follow-up was found to be a useful means of obtaining 'real -life' usage data on the switched product, diclofenac.

KEY POINTS

- More medicines are being reclassified from prescription-only to non-prescription availability.
- Little is known about how these medicines are used in the non-prescription setting, and conventional surveillance methods may be inappropriate.
- The current study has demonstrated the potential benefits of using pharmacies in the collection of 'post-reclassification' surveillance data.

ACKNOWLEDGEMENTS

The authors acknowledge the assistance of the pharmacists throughout New Zealand who were involved with recruitment. The research was conducted with the financial support of Novartis New Zealand Limited (formerly Ciba-Geigy New Zealand Limited).

REFERENCES

1. Blenkinsopp A, Bradley C. Patients, society, and the increase in self-medication. *BMJ* 1996; **312**: 629–632.
2. Bradley C, Bond CM. Increasing the number of drugs available over-the-counter: arguments for and against. *Br J Gen Pract* 1995; **45**: 553–556.
3. Gossel TA. Implications of the reclassification of drugs from prescription-only to over-the-counter status. *Clin Ther* 1991; **13**: 200–215.
4. Ryan M, Yule B. Switching drugs fro prescription-only to over-the-counter availability: Economic benefits in the United Kingdom. *Health Policy* 1990; **16**: 233–239.
5. Smith MC. Prescription to OTC switches: Reflections and projections. *Drug Topics* 1998; **142**(14): 70–79.
6. Barber N. Drugs: from prescription only to pharmacy only. *BMJ* 1993; **307**: 640.

7. Volans G. Monitoring the safety of over the counter drugs. *BMJ* 1987; **295**: 797–798.
8. Schmid B. The safety assessment of over-the-counter products. *Arch Toxicol* 1995; **17**: 305–311.
9. Chaplin S, Blenkinsopp A. Clinical trials in community pharmacies: Too little is known about over-the-counter drugs. *BMJ* 1992; **304**: 63–64.
10. Andersen M, Schou JS. Are H_2 receptor antagonists safe over-the-counter drugs? *BMJ* 1994; **309**: 493–494.
11. Gore MR, Thomas J. Nonprescription informational services in pharmacies and alternative stores: Implications for a third class of drug. *J Soc Admin Pharm* 1995; **12**: 86–89.
12. Hawker G. Prescribing non-steroidal anti-inflammatory drugs — what's new? *J Rheumatol* 1997; **24**: 243–245.
13. DeArmond B, Francisco CA, Lin J-S, *et al*. Safety profile of over-the-counter naproxen sodium. *Clin Ther* 1995; **517**: 587–601.
14. Lanza FL, Codispoti JR, Nelson EB. An endoscopic comparison of gastroduodenal injury with over-the-counter doses of ketoprofen and acetaminophen. *Am J Gastroenterol* 1998; **93**: 1020–1023.
15. Emmerton LM, shaw JP, Tucker IG. Pharmacy-based surveillance of Cataflam® (diclofenac potassium): A pilot project. *NZ Pharm* 1995; **15**(1): 22–26.
16. Henry DA, Sutherland D, Francis L, Newcastle Retail Pharmacy Research Group. The use of non-prescription salbutamol by asthmatic patients in the Hunter valley, New South Wales. *Med J Aust* 1989; **150**: 22–26.
17. Gibson P, Henry D, Francis L, *et al*. Association between availability of non-prescription β_2-agonist inhalers and undertreatment of asthma. *BMJ* 1993; **306**: 1514–1518.
18. Nykamp D, Barnett CW, Hooper C. Risk of adverse drug events related to ibuprofen use in a community sample. *J Pharm Technol* 1994; **10**: 110–114.
19. Brånstad JO, Kamil I, Lilja J, Sjoblom M. When topical hydrocortisone became an OTC drug in Sweden — a study of the users and their information sources. *Soc Sci Med* 1994; **39**: 207–212.
20. Shaw JP, Ferry DG, Pethica BD, Brenner D, Tucker IG. Usage patterns of transdermal nicotine when purchased as a non-prescription medicine from pharmacies. *Tobacco Control* 1998; **7**(2): 161–167.
21. Sift R, Van Staa T-P, Abenhaim L, Ebner D. A study of the utilisation of non-steroidal anti-inflammatory drugs using a pharmacy-based approach. *Pharmacoepidemiol Drug Safe* 1995; **4**: 225–230.
22. Noyelle R, Crossland D, Pickvance N. Ibuprofen, aspirin and paracetamol compared in a community pharmacy. *Pharm J* 1987; **238**: 561–564.
23. Quick J, Blenkinsopp A. A community pharmacy study to compare the control of hay fever symptoms by astemizole 10 mg and terfenadine 120 mg. *Pharm J* 1991; **246**: 272–275.
24. Sonderskov J, Olsen J, Schroe S, Meillier L, Overvad K. Nicotine patches in smoking cessation: A randomized trial among over-the-counter customers in Denmark. *Am J Epidemiol* 1997; **145**: 309–318.
25. Cantrill JA, Vaezi L, Nicolson M, Noyce PR. A study to explore the feasibility of using a health diary to monitor therapeutic outcomes from over-the-counter medicines. *J Soc Admin Pharm* 1995; **12**: 190–197.
26. Bond CM, Bradley C. Over-the-counter drugs. The interface between the community pharmacist and patients. *BMJ* 1996; **312**: 758–760.

