Medical-Legal Aspects of Drugs

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Chapter 11

Medicinal Drugs: Labels and Warnings

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Synopsis

11.1 Introduction

A. Problem background

Traffic crashes in the fifteen member states of the European Union (EU) lead to 50,000 fatalities and more than 1.5 million injured people each year. Based on current statistics, one out of three Europeans will one day be hospitalized as a result of a traffic crash (Cornelissen, 1997). These figures conceal immeasurable loss and human suffering, as well as considerable loss in economic terms, annually costing our society over 70 billion ECU (*White Paper on Transport Policy*, COM 92/494, European Commission).

It is widely recognized that alcohol use is a causal factor in 20 to 40 percent of fatal road crashes. Medicinal drugs are also known to impair driving ability. Available data allow one to conclude, for example, that use of the most frequently prescribed benzodiazepine tranquilizers more than doubles the risk of injurious accidents (Ray et al., 1992). Neutel (1995) reports extremely high relative risk ratios during the first two weeks of treatment with these drugs. Specifically, there is a five to six fold increase in crash risk, which is comparable to the increased risk with 0.10 percent blood alcohol concentration (BAC).

Impairing medicines are used by an average of ten percent of the adult driver population in the EU. If these users are driving with even twice the risk of being involved in a traffic crash, it can be estimated that the drugs are causing 4,500 deaths, 135,000 injuries and 6.3 billion ECU damage to society each year (De Gier, 1995). This kind of information is critically relevant to traffic safety and needs to be available to physicians and patients. From a public standpoint, the increased relative risk clearly is unacceptable, and policy measures are needed in this area.

B. Labeling to communicate risk

It is widely acknowledged that patients require counseling about the effects of medicinal drugs on driving skills, but it is unrealistic to rely upon the advice of drug manufacturers for the information for that purpose. This problem is well known to prescribing physicians and dispensing pharmacists. Too often the warnings provided in package inserts are vague or illogical, and they sometimes are actually misleading.

To illustrate these kinds of problems, a typical general warning for physicians, pharmacists and patients of a drug's adverse effects on the central nervous system lists "anxiety, confusion, dizziness, euphoria, floating feeling, insomnia, nervousness, paresthesia, somnolence and tremor." An additional warning notes that the "drowsiness and dizziness related to use of the drug may impair mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving or operating machines." In addition to this very general caution, a more specific warning alerts patients to "use caution in such activities until their individual responses to that drug have been well stabilized."

A question arises as to whether the physician's instruction to patients really should be limited to a warning to "allow time to stabilize your re-

sponses to the drug before driving." The answer is, "Certainly not." A more effective instruction to the patient, and the most reasonable interpretation of the expected drug effects, would be to advise the patient to avoid driving for a specific time period after each dose of the drug. A major impediment to appropriate warnings, however, is that the drug regulatory authorities approve manufacturers' inadequate statements. Thus, it becomes the physician's responsibility to properly advise the patient. In this chapter opportunities for improving this situation will be discussed. After the description of current labelling systems, primarily based on European experiences, the roles of health care providers and patients will be highlighted.

11.2. Current Labeling Systems

A. Warning systems for drugs and driving

Information about increased crash risk as a consequence of using hazardous therapeutic drugs must be meaningfully communicated to patients. The simplest way to achieve this would be by means of clear warning labels on the packages. Most EU member states, however, do not require exterior warnings on packaging, and patients are informed about impairing effects only by the package insert. Since 1992, European legislation has required warnings regarding the ability to drive or use machines, written in lay language, to be part of the content of the patient drug information leaflet (Council Directive 92/27/EEC).

Exterior warning labels on packaging were introduced in the Netherlands and the Nordic countries in the early seventies and eighties, respectively. A warning system was introduced in 1973 as a practice guideline by the Dutch professional organizations of physicians and pharmacists. It consists of a list of drugs that can adversely affect driving. The listing is based on each drug's pharmacodynamic profile or its therapeutic class. A committee of the Royal Dutch Society for the Advancement of Pharmacy (KNMP) made the label assignments for all drugs licensed in the Netherlands.

Pharmacists are advised to attach a yellow label with black letters for drugs that can adversely affect driving performance. In addition, two other possibilities exist under the practice guideline. One option is that if the physician does not want his patient to be warned of driving impairment, he may tell the pharmacy not to attach the yellow label. Also, if the physi-

cian does not want his patient to drive at all, he may ask the pharmacist to attach a red label with text stating that driving is forbidden while using the drug. This prohibition is possible, because Dutch traffic law prohibits driving a vehicle while under the influence of a drug that the driver knows, or should reasonably know, can impair driving performance to a degree that makes him or her unable to drive safely.

In practice, only the use of the yellow label has been accepted and implemented. With the computerization of pharmacy practices, that warning is nowadays routinely printed on the dispensing label, together with other directions for use of the medicine. At the present time, yellow labels are used as extra warnings by approximately two-thirds of Dutch community pharmacists. Physicians never request that the warning should not be affixed, nor do they request the red label, which is presently unknown to many pharmacists.

A package label warning was introduced in Norway in 1981, and it was adopted by Denmark, Finland, Iceland, and Sweden in 1983. A committee of experts created the label, and the Nordic Committee on Medicines oversees the warning system. A label showing a red triangle is printed by the manufacturer on all packages of drugs in the category "especially dangerous," which includes sedative-hypnotics, opioid analgesics and antitussives, antihistamines, some anti-epileptics, centrally acting muscle relaxants and psychostimulants. At the request of the prescribing physician, the label may be affixed to drugs within another category entitled "potentially dangerous," which includes nonnarcotic analgesics, anti-diabetics, anorexants, anti-Parkinson's drugs, hypotensives, neuroleptics, antidepressants, anticholinergics and opthalmologicals. Initially, in dispensing medication labelled this way, pharmacists were also required to provide the patient with a special leaflet containing additional information. This requirement, however, was dropped after three years, because the additional information was judged redundant.

Other systems have been proposed in Belgium, Spain and France. Detailed information is available, however, only for the system proposed in France where it was decided two years ago to have all packages of psychotropic medication show a warning symbol (red triangle with a black care in the centre).

B. Deficiencies of the present systems

The dichotomous systems introduced in the Netherlands and the Nordic countries fail to distinguish either between drugs in the same therapeutic class that could have markedly different effects on driving ability or between different doses of the same drugs. These and other deficiencies are probably responsible for the fact that most patients do not alter their driving behaviors in any significant way as a direct result of the labels. A small-scale questionnaire survey of Dutch patients who were receiving psychotropic medications revealed that 75 percent of them did not respond appropriately (Stout and De Gier, 1982). Patients reported that they used less of their medications, interrupted the dosing regimens, or simply ignored the warning because they did not realize it applied to them.

A second study was carried out subsequent to a general public campaign concerning the influence of drugs on driving (De Rooij and Leufkens, 1988). A questionnaire was distributed to 1,043 patients who were receiving a drug with a yellow label. This study revealed that only 30 percent of the respondents had changed their behavior towards driving. The changes included not driving, driving less, and driving more carefully.

Faced with a difficult decision regarding labelling for the new antihistamine, cetirizine, the KNMP has decided to defer making the decision. It awaits categorization of the drug according to a somewhat more informative Pan-European warning system of the EU's Medicines Evaluation Agency (EMEA).

The Swedish national pharmacy company Apoteksbolaget AB published an evaluation of the Nordic red triangle system in 1987 (Lisper, 1987). A survey of a sample of the general public was conducted by questionnaire to investigate understanding of the meaning of the red triangle. The question was asked, "If you see a red triangle on an medicine box, what does that mean to you?" About half of the respondents said they understood it to mean that one should not drive a car when taking such a medicine. The other half thought it was similar to other warnings, such as "keep out of reach of children," "dangerous" or "poison".

C. Initiative toward a new system

In 1987 the need for an improved warning system for drugs and driving was strongly expressed by a Dutch National Task Force of experts in

medicine, pharmacy, law and traffic safety (Van Gruting and de Gier, 1990). The task force emphasized that new scientific knowledge should be applied in compiling drug lists and in improving prescribing and dispensing practices. Consequently, the implementation of a three-tier warning system for identifying the driving hazard potential of every new drug has been proposed by an international group of experts. In consensus, the expert panel proposed that the system be a single European drug label warning system (Wolschrijn et al., 1991). Implementation of such a system would increase the awareness of the general public, healthcare providers and policy makers. To the extent that it might result in healthcare providers regularly prescribing and dispensing the least impairing of several equally efficacious medicines, a major contribution to preventing driving while impaired by medicinal drugs would be expected.

11.3 Opportunities for Improving Label Warnings

A. European Union's *Note for Guidance* . . .

The new warning system based on consensus among scientists and introduced in 1991 (Wolschrijn et al., 1991) was meant to replace the dichotomous systems. The major improvement of the system was its scheme for categorizing drugs according to their potential for impairing driving skills. The European drug regulatory authorities adopted a *Note for Guidance for the Summary of Product Characteristics*, SPC (III/9163/90-EN, final approval by the Committee for Proprietary Medicinal Products 16 October 1991).

In 1998 a survey was conducted to determine how responsible regulatory authorities in the different European countries have reacted to this *Note for Guidance* (De Gier, 1998). The report of survey findings highlights the European ministers of transport resolve that EU member states should encourage the systematic printing of a warning symbol on the packaging of medicines likely to impair driving (ECMT/CM 93/5/Final). The *Note for Guidance* provides the framework needed to categorize drugs in order to provide three different warning symbols reflecting the following categories of Article 4.7 of the SPC ("Effects on ability to drive and use machines"):

used for practical reference in addition to the statements on side effects. They believed a category would give the "right weight" to the descriptions, but they also indicated that for that purpose, the terminology such as minor, moderate and severe needed to be defined. Hence, the recommendation is first of all to discuss with the EU's regulatory authorities how a three-tier categorization system can be used as practical reference in order to improve warnings for patients.

C. Procedures for assessing warnings and guidelines for allowing categorization

Generally speaking, the drug regulatory authorities review the data provided by the drug manufacturers and assess whether these data support statements in the *Summary of Product Characteristics*. There are no criteria stipulating the number of reports or the kinds of tests that are needed as a basis for their assessments. It is a case-by-case assessment. Furthermore, the methodology of experimental research on drug effects is still poorly described, although adequate descriptive information exists based on the consensus of scientific opinion.

Some harmonization has been achieved, however. For example, in the provision of a specific *Note for Guidance on the Summary of Product Characteristics* of benzodiazepines as anxiolytics, the recommendation for information to be contained in the warning about the effects of these drugs on the ability to drive and use machines has been standardized. It offers no opportunity, however, for distinguishing between various benzodiazepines when data from experimental or pharmacoepidemiological research demonstrates different behavioral toxicities. Unfortunately, this situation has not been recognized by the drug regulatory authorities as an obstacle to accurate categorization. Hence, it is recommended that better guidelines be established to assist drug manufacturers to select appropriate drug-testing methodologies and to reconsider the use of standard information for the warning section in the *Summary of Product Characteristics*.

D. Failure to categorize

A major problem in the categorization of drugs will be the lack of support from the drug manufacturers who have to submit the relevant data. Even if a standardized methodology is applied to test a drug's impairing proper-

ties, there will always be discussion with drug companies. If their drug has been found to be impairing, the issue will be whether it will be assigned to a different category than non-impairing drugs belonging to the same therapeutic class. Drug manufacturers can be expected to fully approve categorization only when their drug can be distinguished as being safer than competitors' drugs.

Some drug regulatory authorities indicated that experimental research alone is not sufficiently convincing evidence to support the formulation of different warnings. They suggested that revision of the warning system should be based on results obtained from studies of large populations who have used the drugs. They propose that the study investigators should assess the risk potential of accident involvement for each individual drug. It is unclear whether there will be a need for the European Medicines Evaluation Agency (EMEA) to provide specific expertise in this area. EMEA is responsible for international harmonization in the approval of pharmaceutical products and also for coordination of national activities in the area of post-marketing surveillance. It is an EMEA responsibility to ensure the safety of medicinal products circulating within the Community. Although most regulatory authorities feel much more comfortable selecting their own experts, some of them would welcome specific expertise provided by EMEA. It is recommended that EMEA initiate an investigation to decide whether or not it should coordinate large-scale, case controlled pharmacoepidemiological surveys. These would use existing databases in different Member States to determine the relative risks of traffic crashes for users of all drugs identified as potentially dangerous.

E. Examples of warnings in the summary of product characteristics

It is an exception, rather than the general practice, whenever the statement in the driving warning is explicit. An example of such an exception is the clear statement in Finland for buspirone (an anxiolytic): "Does not affect driving . . ." (See Table 11.1). The survey found that most driving warnings provided by the different regulatory authorities were vague, illogical and sometimes misleading. In general, the pattern of the warming is the following. The information starts with a list of the drug's effects on the central nervous system. It then states that these effects may impair mental and physical abilities required for the performance of potentially hazard-

ous tasks. The warning ends with the advice that patients should be told to use caution in such activities until their individual responses to the drug have been well established. There is no advice about how to assess or recognize the individual patient's susceptibility to drug impairment.

Table 11.1
Examples of Discrepancies in the Driving Warnings in Different Member States

Drug	EU Member State	Driving Warning in the SPC
Citalopram (anti-depressant)	Spain	Does not impair . . . However, patients should be cautioned . . .
	United Kingdom	Does not impair . . . However, some impairment expected . . .
	Belgium	Does not impair . . . Does not potentiate alcohol effects . . .
	France	Does not show impairment but may affect skills . . .
	Netherlands	May impair . . . Patients should be cautioned . . .
Piracetam (nootropic)	Finland	Some patients may experience drowsiness . . . Caution advised for...
	Belgium	(No data provided in the SPC)
	United Kingdom	No experience on driving . . . Caution should be exercised . . .
Topiramate (anti-epileptic)	France	(Long list of side effects) . . . Patients should be warned . . .
	Finland	May impede motor skills . . .
	United Kingdom	Drowsiness is likely to occur . . . More sedating than other anti-epileptic drugs . . . Could be potentially dangerous . . .
	Belgium	Drowsiness and dizziness are minor side effects . . . But patients should be warned . . .
Lamotrigine (anti-epileptic)	Netherlands	Due to CNS effects patients should be cautious . . .
	Finland	Because of individual response patient has to consult his doctor
Nefazodone (anti-depressant)	United Kingdom	Modest to no impairment . . . However, patients should be cautioned . . .
	Finland	Take into account that the ability to react will slow down . . .
Reboxetine (anti-depressant)	Germany	Does not impair . . . However, patients should be cautioned . . .
	Finland	Patients must be warned about effects on driving . . .
Buspirone (anxiolytic)	Spain	Patients should be warned about effects and advised not to drive . . .
	Finland	Does not affect driving . . .

It would be advisable to investigate in the different Member States what impact present package insert warnings have on physicians' attitudes towards instructing their patients about driving or operating machines, and on patients' intentions and attitudes about changing their customary behaviors while taking the drug. The results will constitute much needed feedback to drug regulatory authorities and drug companies who are responsible for providing the warnings.

F. Opportunities to improve warnings

A slight majority of survey respondents believe that a categorization system could improve the effectiveness of warnings, compared to the long lists of side effects that are currently provided as warnings. The new European *Guideline* on this subject (III/5218/97, final approval September 1998) provides an opportunity to improve the readability of the label and package inserts with specific guidelines for certain categories of medicinal drugs. Clear statements are prescribed, and pictograms may be used as an additional measure if they make the message clearer to the patient.

There are current movements towards categorization systems for the purpose of improving warnings in at least five member states: Belgium, Germany, the Netherlands, France and Spain.

In 2001 Spain became the second country in Europe to officially introduce a categorization system for drugs having a potentially dangerous effect on driving (Del Rio Garcia, 2001). Belgium was the first country that officially introduced the categorization system in April 1999, at the time that the traffic law was changed into a "zero tolerance" law for illicit drugs (Charlier et al., 1999). Medicinal drugs were not included in this new law, but the Belgian minister of transport considered these to be dealt with by preventive measures, such as prescribing and dispensing guidelines and a clear patient information leaflet. Furthermore, professional organizations in these countries have applied the same system in their efforts to support physicians and pharmacists in selecting relatively safer drugs for patients who drive.

The categorization system was originally proposed in 1991 by a group of international experts who wanted a system allowing health care providers and patients to understand more easily the severity of impairment by medicinal psychotropic medicines (Wolschrijn et al., 1991).

Table 11.2

Category	Impairment description for medicinal drugs	Comparison with Blood Alcohol Concentration (BAC)
I	Presumed to be safe or unlikely to produce an effect	Equivalent to BAC < 0.5 g/l (<0.05%)
II	Likely to produce minor or moderate adverse effects	Equivalent to BAC 0.5–0.8 g/l (0.05–0.08%)
III	Likely to produce severe or presumed to be potentially dangerous	Equivalent to BAC > 0.8 g/l (>0.08%)

In order to make the users of the categorization system aware of the meaning of each category, a comparison to the effects of alcohol, which are well known, was suggested by researchers in experimental psychopharmacology in the Netherlands, based on the views on test validation expressed several years ago (O'Hanlon, 1986). Data collected in experimental research, in which over-the-road driving tests have been applied with most frequently used medicinal drugs and alcohol (as "calibration"), have allowed researchers to interpret weaving effects by any drug as equivalent to that produced by a particular blood alcohol concentration (see Table 11.2).

The most important advantage of the three-tier system over "older" dichotomous drug class-based systems or systems based on quotations of long lists of side effects is the focus on the least impairing medications in each therapeutic class.

Since these initiatives will have an effect on the views of patients, physicians and pharmacists, it would be advisable for them to be in accordance with present European Directives and Guidelines aimed at improving the readability of labels and package inserts. Categorization and warning symbols, based on scientific consensus, have been shown to be feasible. By investigating the acceptance of a new warning symbol among patients, health care providers and drug manufacturers, drug regulatory authorities could become more proactive in response to the actual needs of those who use the information presented in the package inserts.

11.4 The Role of Healthcare Professionals

Standard protocols are followed in medical care for diagnosing and treating various diseases and conditions. In those cases where medication is

selected as the preferred treatment option, medicines with known side effects that could harm the patient or diminish the drug's action should be avoided. It now is becoming standard pharmaceutical practice to follow up patients who report drug related problems that caused either treatment failure or harm to the patient (Cipolle et al., 1998; Van Mil, 2000).

Special attention is normally given to patients receiving a drug for the first time. In cases in which pharmacists have built trusting relationships with patients, it is feasible to extend their services to include a duty of care for the safe use of medication. Such pharmaceutical care is being well received not only by pharmacists but also by health care authorities in many European countries, the USA, and Australia. These authorities are aware that valuable pharmaceutical knowledge has been under-utilized for many years.

A. Guidelines for prescribing physicians and dispensing pharmacists

Guidelines for prescribing and dispensing practices must ensure that patients receive the maximum benefit of extant knowledge about drugs. Ideally, all advice given to patients will have the approval of the respective professional organizations of physicians and pharmacists. Educators and trainers should be involved in teaching about this process, so that health care providers enter their professions with an understanding of their responsibilities and the advice they should give. In addition, present knowledge of drug categorization should be used to adjust the existing guidelines for all major complaints and illnesses for which psychotropic drugs are prescribed. In other words, if a psychotropic medication is the selected treatment option, the guidelines must document the benefits of using the least impairing drug within that therapeutic class.

B. Consumer and patient education

Patient education has to be a substantial part of the prescribing and dispensing guidelines. Patients require clear instruction about how to recognize undesirable side effects of a drug. They need to understand how their skills may be affected at the initiation of treatment, as well as at all follow-up visits if medications are prescribed repeatedly. The information should be presented both orally and in writing for maximum effectiveness. In rational prescribing and dispensing the following key messages can be de-

Table 11.3
Guidelines for Prescribing and Dispensing Potentially Impairing Medicines

	Prescribing Guidelines	Dispensing Guidelines
1.	Realize that the use of some psychoactive drugs has been associated with an increased risk of causing an injurious accident and that patients should receive this information.	Discuss with prescribing physician what patient information (written and oral) should be provided at the first delivery of a particular impairing drug.
2.	Consider an alternative in the light of experimental research showing large differences between the effects on driving performance of various drugs within the same therapeutic class.	Inform the prescribing physician that alternative drugs exist in case a drug in class II or III has been prescribed, and inform the patient.
3.	Start with the lowest doses of psychoactive medical drugs and whenever possible avoid multiple dosing over the day.	Advise the physician to prescribe the lowest effective dose of a particular psychoactive medicinal drug and to avoid multiple dosing over the day. Inform the patient.
4.	Do not reflexively "double the dose" if patients fail to respond to psychoactive medication.	Advise the physician to try another drug if the patient reports a lack of efficacy after beginning treatment and inform the patient. If higher doses are needed advise the patient to use the largest part before sleep.
5.	Avoid prescribing different psychoactive drugs in combination.	Explain to the patient that poly-therapy with psychoactive drugs is always an experiment with the patient's safety and to avoid driving if treatment cannot be adjusted.
6.	Do not rely upon the manufacturers' advice for counselling patients about the effects of drug upon driving	Explain to the patient why warnings provided by the manufacturer about their drug's effects on driving are vague, illogical and sometime misleading.
7.	Advise patients concerning the ways they can minimize the risk of causing a traffic accident if it is impossible to avoid prescribing an obviously impairing drug or one with unknown impairing potential (See Table 11.4).	Advise the patient the ways they can minimize the risk of causing a traffic accident if they have to use a drug with an impairing potential (See Table 11.4).
8.	Monitor the patient's driving experience with the drug.	Monitor the patient's driving experience with the drug (e.g., at the first refill) and report back to the physician or ask the patient to inform the physician

Table 11.4
Prescribing and Dispensing Information: Guidelines by Drug Class

Drug Class (Little/no impairment)	Risk Factors	Prescribing Information	Dispensing Information
Hypnotics			
Take at night. Temazebpam 10 mg Lormetazepam 1 mg Zolpidem 10 mg	Combination with other psychoactive drugs Liver and/or renal dysfunction Elderly patients: 1/2 the normal dose	Avoid prescribing for longer than 2–4 weeks	Avoid alcohol while taking this drug. Recognize signs[1] of impaired driving. Stop driving if any occur. Avoid taking longer than 2–4 weeks and do not take more than one at night.
Tranquilizers			
No impairment Buspirone 10 mg	No specific risk factors known	Avoid combination with selective serotonin reuptake inhibitors (SSRIs) because of reduced therapeutic effect. Can combine for one week with oxazepam 10 mg t.d.s. if therapeutic response is inadequate (forbid driving).	Avoid alcohol while taking this drug. Recognize signs[1] of impaired driving. Stop driving if any occur.

fined as essential parts (general and drug specific) of the guidelines to be developed for some frequently used therapeutic drug classes (O'Hanlon, 1995; ICADTS Working Group Report on Prescribing and Dispensing Guidelines for Medicinal Drugs Affecting Driving Performance, 2001).

The prescribing and dispensing information needs to include drug class-specific guidelines. Table 11.3 presents examples of specific guidelines. They should include identification of the least impairing drugs within the class, risk factors with each, together with standard prescribing and dispensing information. Although it will be impossible to recommend an alternate drug if the class does not include any really safe drugs (e.g. the hypnotics), there clearly are safer alternatives for anxiolytics and antidepressants that can be recommended. For example, selective serotonin reuptake inhibitors are safer antidepressants that produce little or no im-

pairment of driving performance, as shown in experimental and epidemiological studies (Ramaekers, 1998; Barbone et al., 1998). These drugs may also be effective in the treatment of anxiety disorders (Ballenger, 1999). Another safer alternative in treating generalized anxiety disorders is venlafaxine, an antidepressant that acts by selectively inhibiting serotonin and norepinephrine reuptake (O'Hanlon et al., 1998).

11.5 Conclusions

A scenario that will improve the present situation of inefficient warning systems in most countries will be a joint action program decided by the authorities responsible for drug regulation, public and environmental health, and transport safety and consumer affairs together. This action program is required to implement, maintain, and evaluate a new warning system for drugs that affect driving ability based on drug categorization. New partners, in particular the pharmaceutical industry, organizations of physicians, pharmacists and patients, as well as insurance companies, should be invited to take part. These new partners have a greater awareness of health issues as a result of health education campaigns and public information provided through new media, such as the worldwide web. They realize that the health care industry is changing. Prevention and health-related quality of life issues are becoming determining factors for both policy makers and payers of health care costs.

Drug regulatory authorities are key players in the process of restructuring drug testing programs to assess a drug's potential for impairing psychomotor and driving performance. Experts in the field of human psychopharmacology who have assessed the effects of drugs on driving have provided the relevant information needed to perform this task. The impact of these efforts on drug regulation has been noticed, but it has not had a significant effect on improving warning systems for patients who drive. Experts should be more effective in disseminating their research data to the public, health care providers, and policy makers. Physicians and pharmacists can contribute to the use of safer drugs by monitoring patient outcomes with respect to behavioral impairment. By selecting the least impairing drug in their prescribing and dispensing practices, they play a significant role in enhancing public safety. In order to be able to do this, they have to know how to assess the level of impairment caused by each individual drug. This information is already available for many frequently

used "old" and many new medicines. The time has come for patient and consumer organizations to ask who is responsible for not applying this knowledge. It is no option to carry on with the current registration procedures that prevent health care providers and patients from receiving information that would allow them to select and to use the least impairing drug for treatment.

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