Translated from ***Rev Prescrire*** **February 2010; 30 (316): 136-142**

A look back at 2009: one step forward, two steps back

● **In 2009, we examined 104 new brand name products or new indications for existing products in the French edition of *Prescrire*. Only 3 of these 104 "innovations" provided some therapeutic advantage, while 19 had clearly unfavourable risk-benefit balances. Marketing authorisations are failing to adequately protect patients.**

● **A number of cheaper generic versions of useful drugs were introduced to the market, while BigPharma's anticompetitive practices were aimed at slowing the growth of generics manufacturers.**

● **The quality of over-the-counter drugs marketed for self-medication, especially "umbrella" brands, left much to be desired.**

● **Consumer protection is clearly not the primary concern of the European (EMA) and French (Afssaps) drug regulatory agencies. They remain too financially dependent on drug companies; hesitate to withdraw dangerous drugs from the market; and withhold drug safety data.**

● **Other signs of drug companies' excessive influence, at patients' expense, include drug pricing that bears little relation to therapeutic advantage (in oncology, for example); the financial dependence of many patient groups on drug companies; the European Commission's attempts to authorise direct-to-consumer advertising and to allow the pharmaceutical sector to tighten its grip on health information, including pharmacovigilance data.**

● **Governments must assume their responsibilities, and patients and the healthcare profession must resist BigPharma's increasing involvement in all spheres of patient care.**

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In 2009, *Prescrire* published independent assessments of 325 drugs, 91 of which were new products. The latter included 46 products with new brand names, 25 line extensions, and 20 generic drugs with invented brand names (**a**).

The following article reviews the major trends observed in 2009.

Therapeutic advance: the cupboard is bare

Among the 325 products and indications examined in our French edition in 2009, 104 were rated based on the advantage they provided over existing treatments: 46 were new products (including one authorised for two different indications), 31 were new indications, 25 were line extensions, and one product was examined after longer follow-up, with "A second look". We rated 62 of these 104 products as representing "nothing new", including 17 of the 25 line extensions.

Fixed-dose combinations: simple novelties. Among the 46 new brand name products, 7 were fixed-dose combinations of existing drugs. Three were mainly intended for the lucrative market in arterial hypertension: *amlodipine + perindopril* (*Rev Prescrire* 311), *amlodipine + olmesartan* (*Rev Prescrire* 309), and *enalapril + lercanidipine* (*Rev Prescrire* 309). Other fixed-dose combinations included: *calcipotriol + betamethasone* (*Rev Prescrire* 314) for psoriasis; *sitagliptin + metformin* (*Prescrire Int* 101) for diabetes; *timolol + brinzolamide* (*Rev Prescrire* 308) for ocular hypertension; and *follitropin alfa + lutropin alfa* (*Rev Prescrire* 303) for ovarian stimulation.

Therapeutic advance: rare and modest. As in the previous year, we identified no major advances in 2009: none of the new drugs or indications were rated "Bravo" or even "A real advance" based on our at-a-glance rating system (see note **c** of the table on page 92, and page 67), while only 3 "Offered an advantage".

We were unable to reach conclusions ("Judgement reserved") on the possible clinical value of 6 new drugs or indications, due to the lack of available evidence.

Gene therapy failed to live up to expectations in 2009, and no gene-based drugs were authorised in the European Union in 2009 (*Prescrire Int* 104).

Unacceptable drugs: still too many on the market. The drugs we rate as "Not acceptable" are those with an unfavourable risk-benefit balance in one or more indications. In 2008, 23 (19%) out of 120 new drugs or indications were rated "Not acceptable", as was the case for 19 (18%) out of the 104 new drugs or indications in 2009 (see note **d** of the table on page 92). Marketing authorisation procedures are still failing to guarantee patients the protection they are entitled to expect from the licensing agencies (*Rev Prescrire* 304). [see page 91] ▶▶

a- In addition, new indications, and reviews of old indications with a longer follow-up in "A second look", generics, labelling changes, miscellaneous changes, brand name changes, and market withdrawals.

see also page 76

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Drugs with unfavourable risk-benefit balances: market withdrawals are needed

● **In 2009, *Prescrire* rated about 20 new drugs (or new indications for drugs already on the market) as "Not acceptable", because they exposed patients to unjustified or disproportionate risks.**

● **It generally takes several years for regulators to launch a market withdrawal procedure. In the meantime they take ineffective half-measures, such as restricting the indications or reducing the reimbursement rates.**

The high proportion of new drugs and indications with unfavourable risk-benefit balances ("Not acceptable", based on *Prescrire's* rating system, see in this issue page 67) is worrisome. Since the mid-2000s, this proportion has consistently been about 20% (see the table on page 92). There are many other unacceptable drugs, some of which have been around for decades.

Drugs that should be withdrawn: a long list. When a drug is shown to have an unfavourable risk-benefit balance, the only effective way of protecting patients is to take it off the market. But such withdrawals are far too infrequent, and some of these drugs, including high-volume prescription drugs, represent a real danger. We continued to warn our readers about these drugs in 2009, and to demand their market withdrawal:

– cox-2 inhibitors: *celecoxib, etoricoxib* (not yet marketed in France) and *parecoxib*, because they have no proven advantages over other nonsteroidal anti-inflammatory drugs (NSAIDs) in terms of efficacy or gastrointestinal adverse effects but carry an increased risk of cardiovascular and cutaneous disorders (*Rev Prescrire* 311 and 314);

– *nimesulide*, because of the unjustified risk of fatal hepatitis (*Rev Prescrire* 313); *piroxicam*, because of an increased risk of potentially severe gastrointestinal and cutaneous effects (*Rev Prescrire* 312), while neither of these drugs has any advantages over other NSAIDs;

– glitazones: *pioglitazone* and especially *rosiglitazone*, because of their lack of proven advantages in type 2 diabetes, and their poor safety profile (*Rev Prescrire* 306);

– vasoconstrictor decongestant drugs marketed for the common cold, because of their potentially life-threatening cardiovascular adverse effects (*Rev Prescrire* 312);

– *duloxetine*, a psychotropic serotonin and noradrenaline reuptake inhibitor, which has similar efficacy to serotonin reuptake inhibitors (SSRIs) but provokes more serious adverse effects (including a dose-dependent increase in blood pressure and liver damage) (*Prescrire Int* 100);

– *trimetazidine*, a drug licensed for angina, visual disorders, dizziness and tinnitus, because it has serious adverse effects (parkinsonian syndrome, tremor, gait disorders) but no proven efficacy (*Prescrire Int* 100);

– *quinine* (sometimes combined with *hawthorn*), because of its unfavourable risk-benefit balance in the treatment of muscle cramps (*Rev Prescrire* 309).

Dextropropoxyphene: welcome withdrawal planned for 2010. European market withdrawal of *dextropropoxyphene* (sometimes combined with *paracetamol*), a weak opioid analgesic with an unfavourable risk-benefit balance that causes hundreds of deaths each year, is expected in mid-2010 at the latest (*Prescrire Int* 102).

The adverse effects of this drug, marketed for more than 40 years in France, have long been known. However, pending effective action by regulatory agencies, sales continue unabated and patients remain at risk.

Half-measures. When a drug is shown to have an unfavourable risk-benefit balance, the health agencies have a tendency to procrastinate by taking hypocritical half-measures that fail to protect patients:

– lowering their rating for products based on *piroxicam* (*Rev Prescrire* 312, 314) and *rosiglitazone* (*Rev Prescrire* 306, 308) in terms of their medical benefit to patients and reimbursement rate;

– lowering their rating for products based on *celecoxib* (*Rev Prescrire* 314) in France in terms of their therapeutic benefit and reimbursement.

– In the case of *benfluorex* (before its marketing authorisation was suspended in late 2009) and *nimesulide*, the French drug regulatory agency authorised generic versions of these drugs instead of simply withdrawing the originator drugs from the market (*Rev Prescrire* 313, 314, 315).

Action needed. Given these serious failings on the part of the health authorities, it is up to healthcare professionals to stop prescribing these drugs and to systematically report all adverse effects, even those that are already well known.

► **Multiple new indications: HIV/AIDS, psychotropics and cytotoxic agents.** In 2009, "slicing up" of indications, a strategy used to increase product visibility, generally without representing a therapeutic benefit for patients, mostly concerned the following products:
– first-line antiretroviral drugs: *atazanavir* (*Prescrire Int* 101) and *darunavir* (*Rev Prescrire* 309);
– psychotropics: *aripiprazole* for schizophrenic adolescents over 15 years of age, and for acute agitation (*Prescrire Int* 104 and *Rev Prescrire* 312); *duloxetine* for generalised anxiety disorder (*Prescrire Int* 100); oral *risperidone* for aggression in Alzheimer's patients (*Prescrire Int* 104), and injectable *risperidone*, following oral neuroleptic therapy (*Rev Prescrire* 307);
– cytotoxic drugs (this issue page 76).

Children: only one significant advance. We examined 11 new paediatric products, new indications or line extensions in 2009. Despite the financial incentives provided for in the European Paediatric Regulation, clinical evaluation of drugs used in paediatrics is still limited.

The only therapeutic advance observed in 2009 concerned an antifungal drug, *caspofungin*, used as a last resort in children with a rare condition, invasive aspergillosis (*Prescrire Int* 102). The *atovaquone + proguanil* combination can be helpful in treatment of malaria attacks in children weighing at least 5 kg (*Rev Prescrire* 304).

However, most drugs approved for paediatric indications in 2009 do not improve the quality of care. Examples include: *adalimumab* in idiopathic juvenile arthritis (*Rev Prescrire* 306); *atomoxetine* in attention-deficit hyperactivity disorder (*Prescrire Int 105*); *insulin glulisine* in type 1 diabetes in children 6 years of age and older (*Rev Prescrire* 304); and *lamotrigine* for absence seizures (*Prescrire Int* 104). There were too few data to determine the role of *etanercept* in plaque psoriasis (*Rev Prescrire* 309).

Generics: some useful drugs despite anticompetitive practices. A study conducted in 2008 by the European Commission's Directorate-General for Competition showed that companies developing originator drugs engaged in anticompetitive practices towards generics manufacturers (*Rev Prescrire* 307). Such practices carry a high cost, for both patients and society as a whole.

Thirty-four new generic drugs (marketed or soon to be marketed in France) were examined in 2009. About half of them provided some benefits, including *clopidogrel* (*Rev Prescrire* 313), *losartan* (*Rev Prescrire* 311), *topiramate* (*Rev Prescrire* 311) and *valaciclovir* (*Rev Prescrire* 314). In contrast, for two generics the risk-benefit balance is unfavourable: *nimesulide* (*Rev Prescrire* 313), a nonsteroidal anti-inflammatory drug; and *benfluorex* (*Prescrire Int* 105), an amphetamine that was finally withdrawn from the French market in late 2009.

Few biosimilars. Copies of originator biologicals are said to be "biosimilar". In 2009, we examined only 2 such products, based on *filgrastim*, a granulocyte growth factor (*Rev Prescrire* 306) and *epoetin zeta* (*Rev Prescrire* 304).

A copy of *interferon beta* was not granted biosimilar status, because it was manufactured in exactly the same way as the originator drug (*Rev Prescrire* 309).

Whether or not copies of biologicals are considered biosimilar, their risk-benefit balances are comparable to those of the corresponding originator drugs.

High-quality care requires access to data

Since the adoption of European Directive 2004/27/EC on human medicines, EU health authorities have become somewhat more transparent. But bad habits die hard. Citizens, patients and healthcare professionals must maintain pressure on the authorities to ensure their new rights to greater transparency are respected.

Drug evaluation: veil of secrecy. Clinical trials with disappointing results often remain unpublished, unlike those with more favourable results. This publication bias leads to an unrealistic perception of the evidence (*Prescrire Int* 104).

According to a retrospective study, only 17% of phase I trials in healthy volunteers are published, versus none of those with negative results (*Prescrire Int* 105 page 46). Serious adverse effects are not systematically reported in publications of clinical trials (*Rev Prescrire* 305). Some unfavourable data are not submitted to the drug licensing agencies, as in the case of *rofecoxib*, for example (*Rev Prescrire* 303).

Similarly, the discovery in 2009 that 21 trials published in specialised journals had been totally fabricated is hardly reassuring (*Rev Prescrire* 311; 313).

To lift the veil of secrecy on drug evaluation, it is important to cross-check different sources of information, including published trials, regulatory agencies, clinical trial registries, and drug companies.

Access to EMA data: serious failings. A 4-year review of how the European Medicines Agency (EMA) meets its obligations for transparency turned up a series of failures and opacity, including reluctance to provide complete information, delays in responding to requests for information, and refusals to provide national agencies' clinical data and pharmacovigilance reports (*Prescrire Int* 103). Some clinical evaluation and pharmacovigilance data that we requested from EMA were in large part censored. For example, 18 pages out of 28 pages of scientific discussion on *risperidone* were totally or partly blacked out (*Rev Prescrire* 309). In addition, only 3 pages of a 68-page assessment report on *rimonabant* were legible, as the rest had been systematically blacked out, line by line, even including the date of the report (*Prescrire Int* 103).

Afssaps: more thorough publication of assessment data needed. The French drug regulatory agency (Afssaps) is hardly better. The agendas of marketing authorisation and pharmacovigilance committees are not made public, and the minutes of the meetings are only published after a delay of several months. Those of the marketing licensing committee are extremely brief.

Conflicts of interest: regulatory agencies need to improve. Conflicts of interest among members of some EMA committees and task forces are not available online but solely on request from the EMA (*Prescrire Int* 103). The French National Authority for Health (HAS) allows specialists and decision-makers to participate in task forces and steering committees without having to first declare their conflicts of interest, or despite links to companies specifically concerned (*Rev Prescrire* 309).

Self-medication: what about quality of care?

In 2009, the self-medication market, coveted by certain drug companies, saw the introduction of very few truly useful products.

"Over the counter": not the best choices. In 2009, more drugs were added to the list of products available over the counter for the treatment of mild disorders, but few represented the best ►►

Prescrire's ratings of new products and indications over the last 10 years (a)

Prescrire's rating	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Bravo	0	0	0	0	0	0	1	1	0	0
A real advance	4	2	4	4	0	1	1	2	0	0
Offers an advantage	9	11	9	5	6	4	8	14	6	3 (c)
Possibly helpful	24 (b)	17	18	23	12	20	31	27	25	14
Nothing new	53	36	35	34	41	38	69	79	57	62
Not acceptable	2	9	6 (b)	7 (b)	7	19	17	15	23	19 (d)
Judgement reserved	5	7	0	6	4	2	8	3	9	6 (e)
Total	97	82	72	79	70	84	135	141	120	104

a- There is only space in this table to provide the results for the last 10 years. Readers interested in previous years (1981 to 1999) can find the information in Prescrire issue 213 p. 59 and issue 224 p. 56.

This table includes new products (other than generics) and indications intended for patients both in the community and in the hospital setting, and also, since 2005, line extensions (new doses, pharmaceutical forms and preparations of existing drugs), and drugs for self-medication examined in Prescrire. A given product is counted several times if it received different ratings in different indications.

b- Including two jointly marketed products.

c- The drugs concerned include:
– caspofungin as a last resort for children with invasive aspergillosis (Prescrire Int 102);
– thalidomide for first-line treatment of some myelomas in elderly patients (Prescrire Int 100);
– influenza vaccine containing a fragmented virus, with no adjuvant, for type A/H1N1v influenza (Rev Prescrire 313).

d- The drugs concerned include:
– a combination of nicotinic acid + laropiprant for lipid disorders (Prescrire Int 105);
– agomelatine for depression (Prescrire Int 104);
– ambrisentan for grade II pulmonary arterial hypertension (Prescrire Int 100);
– bosentan for grade II pulmonary arterial hypertension (Prescrire Int 100)
– certolizumab pegol as a last resort for Crohn's disease (Prescrire Int 101);
– dapoxetine for premature ejaculation (Prescrire Int 105);
– duloxetine for generalised anxiety disorder (Rev Prescrire 303);
– gefitinib for some forms of non small-cell lung cancer (Prescrire Int 100);
– gemcitabine for some forms of relapsed ovarian cancer (Prescrire Int 102);
– glatiramer for multiple sclerosis (Prescrire Int 104);
–ibritumomab for consolidation therapy of follicular lymphoma (Rev Prescrire 308);
– the combination of levodopa + carbidopa + entacapone, at high (Rev Prescrire 309) and intermediate doses (Rev Prescrire 314) for Parkinson's disease;
– micafungin for severe candidiasis (Prescrire Int 102);
– moxifloxacin for upper genital tract infections (Prescrire Int 103);
– the combination of paracetamol + tramadol in the form of effervescent tablets for pain (Rev Prescrire 314);
– ranolazine for stable angina (Prescrire Int 102);
– rotigotine for restless legs syndrome (Prescrire Int 103);
– topical tacrolimus for the prevention of exacerbations of atopic dermatitis (Rev Prescrire 311).

e- The drugs concerned include:
– caspofungin for suspected fungal infections in children (Prescrire Int 102) ;
– cetuximab for recurrent and metastatic upper respiratory tract and gastrointestinal malignancies (Rev Prescrire 308);
– cinacalcet for primary hyperparathyroidism (Rev Prescrire 308);
– etanercept for plaque psoriasis in children (Rev Prescrire 309);
– temoporfin for upper respiratory tract and gastrointestinal malignancies after failure of standard treatment (Rev Prescrire 308);
– influenza vaccine containing inactivated whole virus for A/H1N1v influenza (Rev Prescrire 313).

► available choice. Examples included: *guaifenesin*, a mucolytic agent for productive cough (*Rev Prescrire* 306); *pheniramine* (combined with *paracetamol* and *vitamin C* in Fervex°), a sedative atropinic antihistamine for runny nose (*Rev Prescrire* 306); and *trolamine* for mild burns and uninfected wounds (this issue page 64).

Drugs "switched" to non-prescription status : a slight advantage with pantoprazole. In 2009, 3 drugs were "switched" from prescription-only to non-prescription status. Two were authorised through a European procedure: *orlistat* for weight loss (*Prescrire Int* 101); and *pantoprazole* for gastroesophageal reflux (*Prescrire Int* 104). *Racecadotril* for acute diarrhoea was authorised through the French national procedure (*Rev Prescrire* 304). Only *pantoprazole* provided a benefit for patients.

In 2009, the European Committee for Medicinal Products for Human Use (CHMP) refused an application to switch *sildenafil* to non-prescription status in erectile disorders, because of its potentially serious adverse effects. This deprived the company of an opportunity to publicise its product, as direct-to-consumer advertising is only authorised for non-prescription drugs in the European Union (*Rev Prescrire* 308).

Proliferation of umbrella brands: danger. So-called umbrella brands gather various products with different compositions, and sometimes, different licensing status, under the same brand name. This is essentially a marketing ploy, based on the choice of easily recognised names. However, umbrella brands can be dangerous, especially when the same drug is available under different brand names (*Rev Prescrire* 307).

Some umbrella brands were expanded in 2009, including: Humex° for sore throat, colds and allergies (*Rev Prescrire* 308, *Rev Prescrire* 312, *Rev Prescrire* 313, *Rev Prescrire* 314); Imo° and Imodium° for diarrhoea (*Rev Prescrire* 307, *Rev Prescrire* 312); and Vicks° for colds and sore throat (*Rev Prescrire* 306, *Rev Prescrire* 311).

Self-medication: we need high-quality products only! Self-medication is useful for treating some mild disorders, provided a pharmacist is on hand to rule out a more serious ailment. And provided patients have access to high-quality products, with more benefits than harms; proper packaging, including a fully informative patient leaflet; labelling highlighting the international nonproprietary name (INN, "a drug's true name"); precise, practical measuring devices for multidose oral solutions; etc. (see the June issue).

A survey conducted by the Toulouse Pharmacovigilance Centre identified a number of errors parents made when treating their children with non-prescription drugs, including administration of the same drug under two fancy names, and use of a measuring device intended for another product (*Prescrire Int* page 28).

The regulatory agencies must carefully select the drugs they authorise for self-medication, and ensure that drug companies market only high-quality products.

Inadequate patient protection

Drug regulatory agencies are mandated to protect patients' health. Unfortunately, they will be unable to fulfil this role as long as they, and many of the experts who sit on their committees, are financially dependent on drug companies (*Rev Prescrire* 306, *Prescrire Int* 100). Many examples of agencies' failure to protect patients were again observed in 2009.

Market withdrawals of harmful drugs: too few, too slow. In 2009, 3 drugs were withdrawn from the European market because of their adverse effects: *benfluorex* (an amphetamine marketed for more than 30 years in France), because of neuropsychological and car-

diovascular disorders (including pulmonary hypertension and valve disease) (*Prescrire Int* 101 and 105); *efalizumab*, a drug authorised 5 years previously for psoriasis, despite its clearly negative risk-benefit balance (*Rev Prescrire* 306 and *Prescrire Int* 103); and injectable *propacetamol*, because of the increased risk of cutaneous disorders compared with injectable *paracetamol* (*Rev Prescrire* 313).

Many more drugs with unfavourable risk-benefit balances remain on the market, some of which have been around for decades (see inset page 90).

Information about adverse effects: withheld or barely visible. Adverse effects identified after a product has been marketed are added to the summary of product characteristics (SPC), but these so-called variations are generally difficult to find, given the large volume of other information in the SPC.

Since 2004, the European Medicines Agency (EMA) has listed "major" variations in a document called "Steps taken after authorisation" on its website. This makes it easier for patients and healthcare professionals to find variations, but the information is often very brief and posted late. We regularly ask the EMA for access to specific data (see inset page 93).

The French Health Products Safety Agency (Afssaps) does not publish a similar list of variations.

Thus, when the French agency does not disseminate information about a specific risk, it can only be identified through detailed comparison of successive versions of the SPC.

Important variations identified in 2009 illustrate the crucial need for transparency and public access to safety data: for example, cardiac disorders with *domperidone* (*Rev Prescrire* 313); increased risk of thrombosis with transdermal patches containing *ethinylestradiol* + *norelgestromine* (*Rev Prescrire* 311); cardiac and visual disorders with *oseltamivir* (*Prescrire Int* 102); a risk of suicide with *varenicline* (*Rev Prescrire* 311); and cardiac and hearing disorders with *sildenafil*, *tadalafil* and *vardenafil* (*Rev Prescrire* 306).

Refusal of marketing authorisation: an effective means of protection. In 2009, we welcomed decisions by the European Committee for Medicinal Products for Human Use (CHMP) to reject a number of marketing applications. Other applications were withdrawn by the companies concerned, after the CHMP issued an unfavourable opinion. These measures protected the public from exposure to unjustified risks.

Examples include: *desvenlafaxine* in depression, because of more cardiac adverse effects than with other antidepressants (*Prescrire Int* 103); *ramelteon*, a melatonin receptor agonist for insomnia, because its adverse effects far outweigh its efficacy (*Prescrire Int* 101).

Pharmacovigilance, "information" and "patient education": not safe in company hands

Several projects envisaged in early 2010 would remove power from the health authorities, healthcare professionals and patients, and place it in the hands of drug companies.

Pharmacovigilance: an unacceptable project for Europe. In late 2008, the European Commission published draft changes to legislation governing the organisation of pharmacovigilance in Europe.

However, several of those proposals would undermine the safety of European citizens, such as more widespread use of the premature marketing authorisation procedure; subcontracting of pharmacovigilance to drug companies (ranging from data collection to interpretation); and an end to mandatory public funding of pharmacovigilance activities.

Experience has shown that drug companies tend to minimise or even conceal information concerning adverse effects. According to the European Commission, adverse drug effects are responsible for at least 5% of hospitalisations and are the fifth cause of in-hospital deaths.

Major amendments to the Commission's harmful proposals are needed to serve the interests of patients (*Prescrire Int* 104 and www.english.prescrire.org under Medicines in Europe).

"Patient information" concocted by drug companies: the return of an unwelcome project. For several years, drug companies and the European Commission's Enterprise Directorate-General have been single-mindedly seeking to obtain authorisation for direct-to-consumer advertising of prescription drugs, which has proven to be highly profitable elsewhere.

To attain this objective, the European Commission has renamed this type of advertising "patient information" (see www.prescrire.org).

Despite strong opposition to this project from other health sector stakeholders in 2007 and 2008, the European Commission is digging in its heels (*Rev Prescrire* 315).

"Therapeutic education": left to drug companies in France. In France, in 2009, "therapeutic education" of patients was enshrined in law (articles L.1611-1 to L.1161-6 of the Public Health Act), with the aim of *"making patients more autonomous, by facilitating their adherence to prescribed treatments and by improving their quality of life"*.

This idea of "therapeutic education" includes programmes of "education", and "training".

The law allows drug companies to contribute to the funding of some of these programmes.

Precisely how the law is implemented must be closely watched: there are too many potential conflicts of interest to leave patient "education" in the hands of the pharmaceutical industry.

Different roles in healthcare. Pharmacovigilance, patient information and patient education are the responsibility of the healthcare authorities, with no interference from the private sector.

Pricing and reimbursement: no relation to therapeutic advantage

Prices granted by governments too often bear no relation to the products' concrete therapeutic advantages over existing treatments.

This is especially true for cancer treatments, where patients have high expectations. In 2009, the price granted for *gefitinib* was equivalent to about 70€ per day of treatment, despite an unfavourable risk-benefit balance in non small-cell lung cancer (*Prescrire Int* 102). A course of *temoporfin* for upper respiratory tract and gastrointestinal tract cancers costs about €5 727, despite this drug's uncertain risk-benefit balance (*Rev Prescrire* 308). And a dose of *ibritumomab* costs €10 900, to which must be added the cost of *rituximab* and *yttrium 90*, for a total of about €15 700, even though the benefit of this treatment in patients with follicular lymphoma has not been convincingly demonstrated (*Rev Prescrire* 308).

In 2009, in France, exceptional reimbursement was granted in certain chronic or rare diseases; this included *thalidomide* in some off-license indications, ▶▶

▶ and products such as sunscreens and sunglasses for patients with xeroderma pigmentosum (*Rev Prescrire* 316).

Advertising and "patient information": still on the rise

After a survey of physician satisfaction with sales reps, a marketing agency revealingly concluded that: *"there is a direct relationship between the number of contacts established by a drug company and the number of subsequent prescriptions"* (*Rev Prescrire* 306).

At the same time, drug companies continued to drive home their advertising messages to patient groups and the general public in 2009.

Companies and patient associations: dangerous liaisons. Drug companies are increasingly focusing their marketing strategies on patient groups (*Prescrire Int* 102). They infiltrate these groups in order to place pressure on regulatory agencies, through the patients, with a view to obtaining more rapid market access and higher prices for their products. Some groups accept drug company funding or participation in "therapeutic education" (*Prescrire Int* 105 page 43). Yet patient groups that accept funding from drug companies risk losing their credibility in the eyes of the authorities, healthcare professionals, patients, and the public.

For example, a bulletin published by one such group contained a drug company proposal to provide information on multiple sclerosis; the company in question markets only two drugs in France, both for multiple sclerosis (*Rev Prescrire* 307).

TV programme sponsorship by drug companies: another propaganda tool. On 1 January 2009, sponsorship of television programmes by drug companies marketing prescription drugs was authorised in France (*Rev Prescrire* 312).

Although it is limited to the promotion of a company's name and image (and does not include its drugs) TV sponsorship is a yet another means of getting the public's attention.

Misleading advertisements: still too numerous. In 2009, we examined 10 drug advertisements aimed at healthcare professionals that were banned by the French drug regulatory agency, mainly because they promoted off-licence use or minimised adverse effects (*Rev Prescrire* 308, *Rev Prescrire* 314).

Many ads placed in professional journals hide or do not mention serious adverse effects.

Thus, publicity for the reimbursement of a so-called third-generation combined oral contraceptive failed to mention an increase in thromboembolic adverse effects (*Rev Prescrire* 313). Similarly, ads for *tramadol + paracetamol* (*Rev Prescrire* 311) and a nasal vasoconstrictor (*Rev Prescrire* 314) listed serious adverse effects in barely visible, small print while claimed benefits were highlighted. Another advertisement, for *fondaparinux*, refers readers to the French datasheet compendium for details of adverse effects (*Rev Prescrire* 303).

Getting back on track

Drug companies are simply filling the void left by the health agencies, which are putting the financial health of the pharmaceutical industry before patients' interests; by patients who are sometimes too naive or inadequately organised; and by healthcare professionals who are sometimes too credulous or "under the influence".

Patients and healthcare professionals must act together to ensure that governments assume their responsibilities, especially when it comes to protecting public health.