New drugs and indications in 2011. France is better focused on patients’ interests after the Mediator° scandal, but stagnation elsewhere

The pharmaceutical market: do not assume that new products represent progress

In 2011, as in previous years, drug companies focused on a few therapeutic fields with high economic potential, such as cancer, cardiovascular disease and ophthalmology (macular oedema and degeneration), but therapeutic advance was rare. Among the 92 ratings for new drugs (with new brand names) and new indications analysed in our French edition in 2011, 53 (58%) represented “nothing new”. Only 3 drugs offered a significant improvement in patient management (“Offers an advantage”; see footnote c in the ratings table page 107). Boceprevir and telaprevir, two drugs representing an advance in the treatment of chronic hepatitis C, were marketed in late 2011 but examined in the January 2012 issue of la revue Prescrire (this issue p. 89-96). They will therefore be included in the review of new products in 2012.

Mostly false innovations. Among the 37 new brand names, there were only 11 new drugs. There were numerous new products masquerading as innovations, mostly with harm-benefit balances that are no better, and sometimes worse, than those of existing treatments. They included:
- 2 recombinant forms of available drugs: corifollitropin alfa, a recombinant FSH for ovarian stimulation (Rev Prescrire n° 329), and conestat alfa, a C1 esterase inhibitor for attacks of hereditary angioedema (Rev Prescrire n° 336);
- 4 old drugs recycled in new indications: amifampridine (3,4-diaminopyridine) used for over 30 years in Lambert-Eaton myasthenic syndrome (Rev Prescrire n° 329), the only drug to offer a slight advantage; fampridine (4-aminopyridine) used to poison birds in the early 1990s, and now marketed for multiple sclerosis patients with gait disorders (Rev Prescrire n° 337); quetiapine, a neuroleptic (Prescrire Int n° 121) approved.


Abstract

- Progress in the pharmaceutical sector accounted for only a tiny proportion of the hundred or so new products and indications analysed by Prescrire in 2011. About 1 in 6 new products had more harms than benefits, while more than half of all new products provided no advantages over existing options. One worrisome trend was the expansion of “umbrella” ranges for self-medication.

- As in previous years, drug regulatory agencies continued to grant marketing authorisation prematurely or on the basis of inadequate evaluation. This was especially true for paediatric medicines, despite some limited progress.

- In the wake of the Mediator° disaster, the French health authorities in charge of patient protection, including the drug regulatory agency, finally reacted by withdrawing many old drugs with negative harm-benefit balances and made an effort to increase transparency and to provide better information on drug-related harms. European authorities showed no signs of similar improvements in early 2012.

- Drug companies continue to promote their products aggressively, which is not in patients’ best interests. The medicalisation of life continues apace, with more and more direct-to-consumer advertising.

- The Mediator° disaster was a wake-up call for French policy makers. In late 2011, several new regulations serving patients’ interests were adopted, including greater transparency and better management of conflicts of interest, but as yet, with no major breakthrough in attitudes and procedures.

since 1997 in the United States and the UK; prucalopride, a stimulator of gastrointestinal motility known since the late 1990s, was approved for chronic constipation in women (Prescrire Int n° 116).

- 3 “me-too’s”: eslicarbazepine, an oxcarbazepine me-too for partial epilepsy (Rev Prescrire n° 331); histrelin, yet another gonadorelin agonist for prostate cancer (Rev Prescrire n° 336); and velaglucerase alfa, a virtual copy of imiglucerase, for type 1 Gaucher’s disease (Rev Prescrire n° 331).

**Drug regulatory agency assessment procedures: uncertainties and inadequacies.** In 2011, Prescrire highlighted weaknesses in the pre-marketing evaluation of several drugs approved by regulatory authorities:
- too few data to reliably determine the harm-benefit balance (“Judgement reserved”, see note e of the ratings table below);
- misuse of statistics, including inherently unreliable subgroup analyses in trials of docetaxel as adjuvant treatment for breast cancer (Prescrire Int n° 117);
- dangerous leniency, particularly the approval of a monoclonal antibody, denosumab, to prevent osteoporotic fractures, despite its numerous adverse effects (Prescrire Int n° 117).

Approximately one in six new drugs best avoided. In 2011, about 1 in 6 new products or indications (16 out of 92, 17%) were rated “Not acceptable” by the Prescrire team, meaning the drug should simply not be used in the indication in question (see note d in the ratings table below).

Healthcare professionals must remember, and notify patients, that marketing authorisation does not necessarily mean that a drug has a favourable harm-benefit balance. See also the inset on page 108.

**Treatment convenience: don’t rely on fixed-dose combinations.** Prescrire’s analysis of new products also covers convenience of use.

Drug companies stress the convenience of fixed-dose combinations, yet such products do not always allow fine dose adjustment and can carry an increased risk of adverse effects and interactions (Rev Prescrire n° 332).

The fixed-dose combination of aciclovir and hydrocortisone for labial herpes has a negative harm-benefit balance (Prescrire Int n° 119). The other combinations marketed in France in 2011 provided no advantages over existing options: amiodipine + telmisartan in hypertension (Rev Prescrire n° 335); dutasteride + tamsulosin in benign prostatic hypertrophy (Rev Prescrire n° 332), and ibuprofen + omeprazole for moderate pain (Rev Prescrire n° 332).

Apart from new oral solutions for paediatric use (see below) and an orodispersible form of vardenfil for erectile dysfunction (Rev Prescrire n° 330), few improvements in the mode of administration were made in 2011. In particular, the intranasal form of fentanyl (Peclet) for cancer pain is no better than existing options (Prescrire Int n° 123).

**Expansion of umbrella ranges, despite the dangers.** More umbrella ranges were marketed for self-medication in 2011, including “Actifed” (Rev Prescrire n° 332 and 338), “Doli°” (Rev Prescrire n° 331), and “Vicks” (Rev Prescrire n° 338), along with the prescription-only “Alko” product line (Rev Prescrire n° 337). Yet these brand names hide a range of very different active ingredients, creating a risk of confusion for patients. These products should neither be prescribed nor dispensed.

**Paediatric drugs: some progress, but inadequate assessment and poor packaging.** The number of medicines authorised for paediatric use has risen slightly since the Paediatric Regulation was adopted in the European Union. Unfortunately, the packaging is often substandard (see in a coming issue) and premarketing assessment is often inadequate. This is the case for abatacept in juvenile chronic arthritis (Prescrire Int n° 328) and atazanavir for HIV infection (Prescrire Int n° 118). A few paediatric drugs, despite their limitations, represent significant advances: 

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- For reason of space this table only shows the results for the last 10 years. The previous years’ results (1981 to 2001) can be found in Prescrire Int n° 58.
- Including two jointly marketed products.
- The drugs were:
  - colchicine in ulcerative colitis and Crohn’s disease in children (Prescrire Int n° 119);
  - loxoforsol in vitamin E deficiency (Rev Prescrire n° 333).

This table shows new products (other than generics) and new indications proposed by drug companies to physicians and pharmacists, for use in hospitals and for the community, and, from 2005 onwards, line extensions (new dose strengths, new forms/presentations of existing drugs) and products for self-medication, rated in our French edition La revue Prescrire. A given product is counted several times if it was rated differently in its different indications.

- The drugs were:
  - aciclovir + hydrocortisone in herpes labialis (Prescrire Int n° 119);
  - bendamustine in second line therapy of indolent non-Hodgkin’s lymphomas and multiple myeloma (Rev Prescrire n° 338);
  - bleoctrizin in malignant pleural effusion (Prescrire Int n° 122);
  - denosumab in postmenopausal osteoporosis (Prescrire Int n° 117);
  - denosumab in prostate cancer related bone loss (Rev Prescrire n° 329);
  - docetaxel in adjuvant therapy for breast cancer (Prescrire Int n° 117);
  - erlotinib in maintenance therapy of non-small cell lung cancer (Prescrire Int n° 120);
  - exenatide in type 2 diabetes in combination with glitazones (Rev Prescrire n° 320);
  - fampridine in multiple sclerosis and walking disorder (Rev Prescrire Int n° 337);
  - lanthanum with more follow up in dialysis patients with chronic kidney failure (Rev Prescrire n° 329);
  - lanthanum in non-diabetic patients with chronic kidney failure (Rev Prescrire n° 329);
  - methotrexate 10 mg, a strong dosage in juvenile chronic arthritis (Prescrire n° 409);
  - mov for fentanyl in community acquired pneumonia and skin infections (Rev Prescrire n° 327 and 328);
  - omeprazole, a weak dosage in severe persistent asthma (Prescrire Int n° 121);
  - prulocaps in prostate with chronic constipation (Prescrire Int n° 116);
  - Bentlnum toxic type A for migraine (Prescrire Int n° 122).

- The drugs include:
  - abatacept in juvenile idiopathic arthritis (Rev Prescrire n° 328);
  - alglucerase alfa in late Pompe disease (Rev Prescrire n° 336);
  - bevacizumab off-label in age-related macular oedema (Rev Prescrire n° 338);
  - cabazitaxel in advanced prostate cancer (Prescrire Int n° 123);
  - quetiapine (Xeroquel LP°) in prevention of depression (Rev Prescrire Int n° 331);
  - rituximab in maintenance treatment of follicular lymphomas (Rev Prescrire Int n° 338);
  - sunitinib in pancreatic neuroendocrine tumours (Rev Prescrire n° 337).
Outlook

A look back at new drugs and indications in 2011

Drugs best avoided yet still on the market in early 2012

Many drugs that have more harms than benefits are still marketed in France, and in some cases, for several decades. The following drugs were examined in Prescrire in 2011, in order of publication:

- nimesulide, a nonsteroidal anti-inflammatory drug (NSAID), because of the risk of liver damage (Prescrire Int n° 116);
- antihistamine antitussives, because of their sedative and antimuscarinic effects (issue 329 p. 179);
- dronedarone, an antiarrhythmic drug, due to a risk of liver damage and cardiovascular disorders (Prescrire Int n° 122);
- terpenes, due to their neuropsychiatric adverse effects (including seizures), especially in young children. In 2011, some medicines for children, mainly suppositories, still contained terpenes. In late 2011, the French drug regulatory agency contraindicated their use in suppositories for children under 30 months (Rev Prescrire n° 340);
- trimetazidine, marketed for angina, dizziness, visual disorders and tinnitus, carries a risk of extrapyramidal disorders, falls and thrombocytopenia (Prescrire Int n° 115). In 2011, the French regulatory agency triggered a referral to the European Medicines Agency;
- pholcodine, an opioid antitussive, because of concerns over a risk of allergy to muscle relaxants used during anaesthesia (Rev Prescrire n° 331). In 2011, the French agency simply ruled that this drug should be available by prescription only, in order to limit its use (Rev Prescrire n° 333);
- oral and nasal vasoconstrictive decongestants (ephedrine, naphazoline, oxymetazoline, phenylephrine, pseudoephedrine and tamaheptane), because of a risk of life-threatening cardiovascular disorders (myocardial infarction, arrhythmia, hypertension). In 2011, the French agency simply demanded a modification in the Summary of Product Characteristics (SPC) (Rev Prescrire n° 335);
- iron dextran, due to a higher risk of hypersensitivity than with iron sucrose (Rev Prescrire n° 335);
- meprobamate is still contained in certain products in France (for gastrointestinal disorders associated with anxiety, and premenstrual syndrome), despite a risk of severe cutaneous and haematological adverse reactions, and a withdrawal syndrome (Prescrire Int n° 123);
- bupropion, an amphetamine derivative, and varenicline, an acetylcholine receptor partial agonist used for smoking cessation, mainly because of cardiovascular and neuropsychiatric disorders (Rev Prescrire n° 328, Prescrire Int n° 124);
- quinine for cramps, because of a risk of haematological disorders, cardiac arrhythmia and hypersensitivity (Prescrire Int n° 115);
- mequitazine, a “sedative” and “atropinic” antihistamine used in allergies, carries a higher risk of cardiac arrhythmia than other antihistamines. In 2011, the French agency simply placed mequitazine on the list of controlled substances (Rev Prescrire n° 337);
- ropinirole, a dopamine agonist used for restless legs syndrome (Prescrire Int n° 115);
- orlistat for weight loss: its adverse effects and interactions largely outweigh a marginal and transient weight loss (Rev Prescrire n° 338);

Since late 2011, some of these products are no longer reimbursed in France, including those based on dronedarone, nimesulide and quinine (for cramps). While the measures limit the consumption of these drugs and, thus, the number of patients exposed, they send a mixed message to patients. Simply withdrawing them from the market is the most effective solution.

Generic drugs with uneven therapeutic value. In 2011, Prescrire examined the harm-benefit balance of 27 generic drugs marketed in France.

Ten of these drugs are useful in certain situations: intradural baclofen for some cases of severe chronic spasticity (Rev Prescrire n° 332); dobetanol, a potent topical corticosteroid for some skin conditions (Rev Prescrire n° 328); daacarbazine for some cancers (Rev Prescrire n° 330); enprostil for pulmonary arterial hypertension (Rev Prescrire n° 328); letrozole in breast cancer (Rev Prescrire n° 333); levetiracetam for various forms of epilepsy (Rev Prescrire n° 336); meropenem (Rev Prescrire n° 337) and teicoplanin in severe infections (Rev Prescrire n° 331), modafinil for narcolepsy (Rev Prescrire n° 329); and valproate (with or without hydrochlorothiazide) for hypertension, heart failure and recent myocardial infarction (Rev Prescrire n° 336).

Many other generic drugs are best avoided, including milnacipran in severe depression (Rev Prescrire n° 338), niandralil in angina pectoris (Rev Prescrire n° 33), and rivastigmine in Alzheimer’s disease and in dementia associated with Parkinson’s disease (Rev Prescrire n° 337).

Marketing applications for generic drugs give regulatory agencies an opportunity to reassess the value of the originator drugs, and to withdraw those with a negative harm-benefit balance. Apparently they are not taking advantage of this opportunity.

Patient protection

In 2011, the French health authorities finally started to react, by protecting patients from several drugs that have more harms than benefits (see page 110).

Market withdrawals: the most effective measure, often taken late. Drug reassessment can result in measures that support patients’ interests, such as market withdrawal of drugs with a negative harm-benefit balance.

In 2011, the French drug regulatory agency finally started to withdraw some of these products, many of which had been on the market for decades:

- buflomedil, a vasodilator marketed for over 30 years (Rev Prescrire n° 327, n° 329);
- the fixed-dose combination of dorzolamide + acetazolamide + acetazolamide, available for nearly 40 years in insomnia (Rev Prescrire n° 335);
- oral ketoconazole, an antifungal drug that can cause severe liver damage (Rev Prescrire n° 335);

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– some products based on meprobamate, used for more than 40 years in alcohol withdrawal, and the fixed-dose combination of meprobamate + acepromazine, used for nearly 50 years in insomnia (Prescrire Int n° 123);
– a fixed-dose combination powder (Paps') of salicylic acid + terpenes (camphor, levomenthol, lavender essential oil) + bismuth + zinc + boric acid, marketed for nearly 50 years for pruritus (Rev Prescrire n° 338);
– products based on piroglitazone, an anti-diabetic drug (withdrawn in France but maintained by the European Commission on the advice of the EMA) (Rev Prescrire n° 335).

Other welcome withdrawals included:
– combinations based on dextropropoxyphene, marketed for more than 45 years for pain relief: withdrawn from the market following a European reassessment (Rev Prescrire n° 327, n° 328);
– celecoxib marketed for more than 45 years for pain relief: withdrawn from the market following a European reassessment (Rev Prescrire n° 327, n° 328);
– oxacillin marketed for more than 40 years in alcohol withdrawal: withdrawn because the company refused to provide supporting data (Rev Prescrire Int n° 121);
– becaplermin (Rev Prescrire n° 335), drotrecogin alfa (Rev Prescrire n° 338) and sitaxentan (Rev Prescrire n° 328) all withdrawn at the request of the drug companies, not the regulatory agencies.

Some decisions supported patients’ interests. Some position statements and decisions taken by drug regulatory agencies in 2011 are worthy of note:
– the French regulatory agency and EMA refused to authorise over-the-counter use of sumatriptan in migraine (Prescrire Int n° 123);
– coherent changes were made to the indications and dosages of penicillins M (doxycillin and oxacillin), useful older drugs, following reassessment by the French agency (Rev Prescrire n° 336).

However, other decisions represented simple half-measures, such as the decision by the French agency to restrict the use of antihistamine antitussives in children less than 2 years old, even though these products have a negative harm-benefit balance in older children and adults. It would have been better to simply withdraw these products from the market (Rev Prescrire n° 329).

Drug regulatory agencies still providing too little information on adverse effects. Information provided by regulatory agencies can help healthcare professionals manage their drug lists and choose the most appropriate drug for each patient. In 2011, the French agency made an effort to improve the quality of this information. For example:
– oleoalcalic liniment: risk of burns when prepared at home by patients (Rev Prescrire n° 328);
– dronedarone: liver damage and heart problems (Prescrire Int n° 120);
– somatropin: increased mortality due to cerebrovascular disorders and bone tumours (Prescrire Int n° 117);
– estradiol: numerous cardiovascular and cutaneous adverse effects, etc. (Prescrire Int n° 117);
– dasatinib: pulmonary arterial hypertension (Prescrire Int n° 120).

However, other important information is buried in the summaries of product characteristics (SPCs), patient leaflets, and the EMAs “steps taken after authorisation” or “assessment reports”:
– tianeptine: cutaneous disorders were added to the SPC, but they are not all mentioned in the 2011 patient leaflet (Rev Prescrire n° 337);
– Natalizumab: data on infections (including progressive multifocal leukoencephalopathy) and hypersensitivity were released in a report from the French Pharmacovigilance Committee (Prescrire Int n° 122);
– thalidomide: data on hearing loss were provided in “steps taken” (Prescrire Int n° 124).

Aggressive drug promotion

Faced with the pervasiveness of drug promotion by pharmaceutical companies and weak regulations, healthcare professionals and patients must remain vigilant.

Do not confuse advertising and information. Healthcare professionals and patients must keep in mind that drug companies’ advertising messages concerning their products should not be considered reliable sources of information. Efficacy is stressed while adverse effects are downplayed or not mentioned at all: for example, varenicline in smoking cessation (Rev Prescrire n° 336 inside back cover), the fixed-dose combination of tramadol + paracetamol for pain (Rev Prescrire n° 329 inside back cover and n° 337 inside back cover), and ketoprofen gel for rheumatic pain (Rev Prescrire n° 328 inside back cover).

Pharmaceutical industry obsession with drug promotion. Drug companies exploit every possible opportunity to promote their products, directly or indirectly, by various means, including:
– patient management software (Rev Prescrire n° 336);
– healthcare professional “training” (Rev Prescrire n° 331);
– gifts to healthcare professionals. It has been shown that even small gifts “of negligible value” elicit reciprocity on the part of the recipient who is often unaware of their influence (Prescrire Int n° 122);
– drug companies have been known to send healthcare professionals falsi-

Questioning French drug policy: a few timid steps taken in 2011

In 2011, the rationale for French drug policy was challenged by the Mediator® disaster (Prescrire Int n° 121).

In March 2011, Prescrire published 57 proposals on its website (english.prescrire.org), based on evidence accumulated over the years, aimed at preventing similar disasters in future and at refocusing national drug policy on public health and patients’ real needs (Prescrire Int n° 116, 121 and 123).

A new law on human medicines was passed in France on 19 December 2011.

Some of its measures will serve patients’ interests:
– better management of conflicts of interest within government agencies;
– more transparent reporting of committee meetings;
– stricter regulation of off-label prescription;
– stricter regulation of medical devices.

However, several important measures were left out:
– development of clinical research more independent of drug companies;
– public access to pharmacovigilance databases, as in countries such as Canada, the United States, the Netherlands and the United Kingdom (Rev Prescrire n° 337 - see this issue page 99);
– requirement to compare new drugs with a standard treatment before marketing authorisation or reimbursement status can be granted;
– measures to promote more convenient treatment and safer packaging (see in a coming issue);
– Better initial and continuing education of healthcare professionals in drug therapy.
A look back at new drugs and indications in 2011

Outlook

Regulation of advertising: doubtful effectiveness. Few unethical ads sanctioned in France. Few advertisements aimed at healthcare professionals were banned in France in 2011, according to the Official Journal (Journal Officiel). As in previous years, the violations were mainly serious, including unethical broadening of indications, promotion of off-label use (including mequital during pregnancy), exaggeration of effectiveness (Rev Prescrire n° 333 and 340). Formal notices to modify these ads are not made public in France. Healthcare professionals were therefore unaware of having been exposed to misleading advertisements.

In Switzerland, despite more stringent regulations requiring that all drug advertisements should be evidence-based, the situation is appalling: half of the claims are not backed up by the cited references, or are based on biased references (Prescrire Int n° 117).

Support the new focus on patients’ interests

In France, the year 2011 was characterised by the lack of major breakthroughs in new drugs or new indications, but there were some welcome decisions aimed at improving patient safety in the wake of the Mediator® disaster, such as market withdrawal of drugs that had more harms than benefits. There was also a trend towards a culture of transparency, and other changes in drug policy, the practical impact and sustainability of which remain to be seen. At the European level, apathy prevailed and no new changes of significance were made to protect patients’ interests.

Drug companies must focus on producing high-quality pharmaceuticals (Prescrire Int n° 124) and ensuring an uninterrupted supply of products with proven clinical value, such as spiramycin oral suspension, which was no longer marketed in France in 2011, and sheep antigalactokin antibodies, that are too often out of stock and are replaced by various brand names and dosages (Rev Prescrire n° 333).

A more general overhaul is needed: healthcare professionals must sever their links with drug companies (Rev Prescrire n° 330); patients must learn not to rely solely on medications (Prescrire Int n° 122); and all those concerned must choose reliable sources of information.

In the wake of the Mediator® scandal: some progress in France, but apathy at the European level

The aftermath of the Mediator® disaster and the serious regulatory shortcomings it revealed led the French authorities to make some improvements to their procedures and decisions in 2011 (Prescrire Int n° 121). For example:
– The French drug regulatory agency finally made a real effort to be more transparent: the working sessions of the marketing authorisation committee are now described in detailed reports, albeit several months later; some (but not all) discussions are now filmed and posted online; and the agendas of the marketing authorisation committee are now made public.
– The French agency triggered reassessment of several drugs at the European level, including pholcodine, pioglitazone (alone or combined with metformin), and trimetazidine;
– The French agency decided to withdraw several drugs with negative harm-benefit balances (see inset page 108);
– The French authorities are taking more notice of recommendations of the Transparency Committee (which assesses the medical benefits of new drugs and advises on drug reimbursement) to stop reimbursing several drugs rated as providing inadequate medical benefit to patients, some of which have been on the market for several years.

In contrast, the European authorities have yet to take action on these points:
– the opacity of pharmacovigilance data persists: for example, information was withheld on the risks of bladder cancer associated with pioglitazone (Prescrire Int n° 123);
– doubts regarding drug safety still continue to benefit drug company profitability rather than patients’ interests: some drugs were kept on the market despite their established harms, including dronedarone, nimesulide, pioglitazone, pholcodine and varenicline (see inset page 108);
– in the public consultation launched by the European Medicines Agency (EMA), posted online in late 2010, the Agency proposed to make head-to-head comparisons with a standard drug the exception in premarketing clinical trials, meaning that placebo-controlled trials would become the rule (Prescrire Int n° 121);
– the European Commission left signal detection and the interpretation of post-marketing surveillance data in the hands of drug companies. These are both key elements of drug safety (isdbweb.org);
– the European Commission continues to insist on removing barriers to direct-to-consumer advertising by drug companies for prescription-only drugs. Following the public outcry in late 2010, the Commission was forced to revise its proposals to allow direct-to-public advertising of prescription drugs, disguised as “information”. However, the amended proposals published in October 2011 still leave the door open to this type of advertising, particularly the proposed legalisation of reminder advertising (a) (english.prescrire.org).

The public must encourage authorities to focus more on patient safety, through actions such as those conducted by the patient group Analyste (victims of Lyell and Stevens-Johnson syndrome) and Act Up (people living with HIV/AIDS), and member associations of the Medicines in Europe Forum (b) (“Prescrire Prize”, prescrire.org).

a Reminder advertising is a marketing practice which aims to familiarise the public with a brand name by using every opportunity to mention the name of the product, including using images of the brand and building an emotional connection with the brand.
b Founded in March 2002, with more than 60 member organisations in 12 European Union member states, the Medicines in Europe Forum is composed of 4 major groups of healthcare stakeholders: patient groups, family and consumer organisations, health insurers, and healthcare professionals (prescrire.org).

fied emails and letters from patients thanking their doctors for having prescribed one of their drugs (Rev Prescrire n° 330);
– “disease mongering”, particularly in the field of psychiatry (Prescrire Int n° 112);
– funding of patient groups. According to a survey by Health Action International (HAI), an international network of organisations and citizens striving, among other things, to promote rational use of healthcare and medicines, most patient groups funded by pharmaceutical companies support direct provision of “information” by drug companies (Prescrire Int n° 122);
– harassment and vilification of scientists by the Danish Association of the Pharmaceutical Industry (Rev Prescrire n° 328);
– etc.