The seven principles upheld by Amalyste

- The patient-advocacy group Amalyste upholds seven principles intended to improve the management of drug-related risks (1).

“The principle of collective responsibility.” This principle flows directly from the concept of the risk-benefit balance (collective acceptance of a risk). Victims must not be left to their fate. In addition, drug-related risk management is a collective issue that must not be left solely in the hands of experts and the pharmaceutical industry. A balanced representation of stakeholders (civil society, citizen groups, the government, the medical and nursing sectors, and drug companies), as well as their independence, must be guaranteed.

The principle of control, knowledge and understanding of risk. The concept of “acceptable risk” implies an obligation to provide the means necessary to document, understand (through research), monitor and control this risk.

The principle of “auditability”. The assessment process must be quantitative and standardised in order to ensure its transparency and subsequent auditability.

The principle of “shared risk”. Drug-related risks, and the way they are insured, must be seen as a collective responsibility, shared by society as a whole.

The principle of risk internalisation. The pharmaceutical industry is part of the private sector. The costs relating to the risks induced by this activity must be internalised and included in the cost of each drug. The pharmaceutical industry is a profitable activity that should be able to integrate, under proper conditions of risk control, the cost of this risk. Furthermore, integration of the cost of this risk in the price of each medication will improve the competitiveness of companies that develop, for a given disease, effective drugs that carry a lower risk of adverse effects.

The principle of full compensation for harm. Harmful effects incurred under collective responsibility must be fully compensated. This implies that the necessary means must be available: compensation provided by the entire community extends far beyond individual responsibility. For instance, in addition to providing individual victim compensation, the community should allocate resources to research and treatment programmes that aim to mitigate the consequences of adverse drug reactions.

The principle of equity regarding the burden of evidence. It may be difficult for victims to prove that an accident was due to a particular drug. They should be given the benefit of the doubt; the first condition for “acceptability” of a severe risk is its very rarity, making it even more difficult for victims to provide conclusive evidence (a)” (1).

The pharmaceutical industry is part of the government, the medical and nursing sectors, and drug companies, as well as their independence, must be guaranteed.

First, the lack of a standard procedure prevents any comparison: it is currently impossible to compare assessments of different drugs on the basis of objective criteria. These assessments are neither comparable nor “auditable”, and are incompatible with any quality-assurance process worthy of the name. Second, the lack of standardised criteria means that it is not possible to set thresholds at which risks are considered acceptable.

What is an “acceptable” risk? Although the French Public Health Code (Article L. 5121-9, R. 5121-45-1 Article, Section L. 5311-1, etc.) repeatedly refers to “the ratio between the benefits and risks” of a drug as the basis for the evaluation that precedes marketing authorisation or market withdrawal, this ratio is never defined in legal terms, and its evaluation, as well as the methods used, are left to the discretion of the French drug regulatory agency or its director. Any reassessment therefore depends solely on the authorities’ goodwill, which is often influenced more by media pressure and lobbying by the pharmaceutical industry than by rational decision-making.

From an ethical standpoint, it is the notion of “sacrifice” that underlies this concept. Yet it has never been properly thought through in terms of responsibility.

Lyell and Stevens-Johnson syndromes

“These serious reactions (fatal in 30% of cases) cause sudden and sometimes extensive detachment of the skin and mucous membranes. Nine in ten cases are due to drug reactions. Some are due to Mycoplasma infection. About a dozen high-risk drugs have been identified (antibiotics, anti-inflammatory drugs, antiepileptics, allopurinol, nevirapine).

Victims must always be managed in a specialised unit. These drug reactions are extremely painful. This is an orphan disease, with 150 cases occurring per year in France and about 1000 in the European Union. It is also a chronic illness: 95% of survivors are left with debilitating and progressive sequelae that totally disrupt their lives.

Identification of the implicated drug is very difficult, as there may be a delay of up to several weeks between drug intake and onset of symptoms, co-administration of several drugs, and inability to carry out rechallenge with the suspected drugs.

Research is inadequate and the mechanisms of these reactions are still not understood” (1).

Sacrifice of the few for the common good

Experts rarely explicitly point out that this “risk-benefit ratio” is assessed statistically, at the population scale, when estimating the collective acceptability of...