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PHARMACOVIGILANCE

French pharmacovigilance: Missions, organization and perspectives

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Summary Pharmacovigilance aims to identify unknown adverse drug reactions once clinical development is complete, in order to promote improved use of drugs, and thus a reduction in risk for every exposed patient. We describe in this article the missions of French pharmacovigilance system, including French drug agency, Regional Centers of Pharmacovigilance, health professionals, pharmaceutical companies, patients and their associations. We also develop the French pharmacovigilance organization, its perspectives and challenges, both in French and European levels.

Abbreviations

ADRs	adverse drug reactions
AFCRPV	French Association of Regional Pharmacovigilance Centers (*Association française des Centres régionaux de pharmacovigilance*)
ANSM	French Agency for the Safety and Health Products (*Agence nationale de sécurité du médicament et des produits de santé*)
ARS	*Agence régionale de santé*
CIOMS	Council for International Organizations of Medical Sciences
CRPV	Regional Pharmacovigilance Centers (*Centres régionaux de pharmacovigilance*)
CTPV	*Comité technique de pharmacovigilance*
EMA	European Medicines Agency
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
NNI	generic products
PBRER	periodic benefit risk evaluation report
PGR	risk management plan (*plan de gestion des risques*)
PMSI	*programme de médicalisation des systèmes d'information*

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PRAC Pharmacovigilance Risk Assessment Committee
PSUR periodic safety update reports
PVWP Pharmacovigilance Working Party
SNIIRAM *Système national d'information inter-régimes de l'Assurance maladie*

Introduction

From the moment marketing authorization is granted for a drug, post-marketing authorization monitoring is put into place, and this involves pharmacovigilance.

Pharmacovigilance aims to identify unknown adverse drug reactions once clinical development is complete, so as to promote improved use of drugs, and thus a reduction in risk for every exposed patient. This field has considerably evolved in the last forty years, as much on French as on European level; indeed, while regulations have been periodically toughened, the methods and tools used in order to better identify, analyse and characterize the signals from pharmacovigilance have also seen great progress.

Each year, around 45,000 [1] adverse drug reactions occurring in France are collected by the Pharmacovigilance Regional Centres. A similar number is managed and sent to the Authorities by pharmaceutical companies.

In France, it is estimated that more than 100,000 hospitalizations [2—4] are caused annually by serious adverse drug reactions, of which 50% are considered avoidable [4]. In addition, in 2014, 1200 medication errors causing adverse reactions were listed [1]. It is likewise thought that 10,000 to 30,000 [2,5] deaths annually could be linked to the occurrence of adverse drug reactions.

These figures alone justify the need for an efficient pharmacovigilance system, in order to ensure correct use of authorized health products.

Definitions and scope

The definitions include:

- adverse drug reaction [6]: harmful and unwanted reaction to a drug or a product, mentioned in article R. 5121-150;
- serious adverse event [6]: lethal or life-threatening adverse event, or event leading to serious or lasting disability or handicap, or causing or prolonging hospitalization, or taking the form of an abnormality or a congenital malformation;
- unexpected adverse event [6]: the nature, severity or evolution of the adverse event does not correspond to the information contained in the summary of product characteristics mentioned in article R. 5121-21 of the public health code;
- misuse: intentional, inappropriate use of a drug or a product in relation, to the authorized or prescribed dosage, the administration route, or the indications, or non-conformity with the marketing authorization, registration terms, or good practice guidelines [6];
- medication error [7]: unintentional act, or omission, during a treatment process using a drug that could be the cause of a risk or an adverse reaction for the patient. Medication errors can either be committed or potential (detected before the drug is administered to the patient);
- pharmacovigilance: field of application [8]:
  - pharmaceutical specialities,
  - blood-derived medication,
  - radiopharmaceutical drugs,
  - homeopathic drugs,
  - magistral or officinal formulae,
  - compendial products,
  - contraceptives,
  - immunological drugs,
  - cellular therapy products subjected to marketing authorisation,
  - gene therapy preparation,
  - xenogeneic cellular therapy preparation,
  - insecticides and acaricides designed to be used on human beings,
  - certain dietary products;
- risk management planning [7]: this contributes to the monitoring of drugs, especially those that have been marketed recently. Risk management planning is required for any drug containing a new active substance. It can also be implemented after marketing, if there are significant changes (new indication, new dosage, new administration routes, new manufacturing process), or if a major risk has been identified. It implies complementary measures as necessary, such as:
  - reinforced pharmacovigilance on some of the risks that have been highlighted,
  - studies on safe post-marketing authorization usage and/or studies on use,
  - measures for minimizing the risks (information documents for health professionals and patients).

Missions and roles of the different protagonists[1] [9]

French agency for the safety of health products (ANSM)

The ANSM is the competent authority in matters of pharmacovigilance. It monitors the safe use of drugs and contributes to their correct use. The ANSM is responsible for implementing and coordinating the national pharmacovigilance system. This system is integrated into a European organization for drug monitoring and authorization.

The drug surveillance and prevention of the risk of adverse effects resulting from their use is based on:

- notification of any adverse events by health professionals, patients and their approved associations, and manufacturers;
- the gathering, processing and evaluation of any information concerning the risks of adverse drug reactions;
- studies or research on safe use of drugs;
- implementation of action required for pharmacovigilance functioning;
- corrective or preventive measures.

Its role mainly consists of:

[1] With courtesy *Agence nationale de sécurité du médicament et des produits de santé* (French Agency for the Safety and Health Products, ANSM).

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