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Editorial Open Access

How to Meet Legitimate Expectations of Patients when Authorized Medicinal Products are not Available

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It is well-known that quality, efficacy and safety have to be guaranteed for medicinal products, but the point is at which level these attributes have to be satisfied. Generally speaking, based on scientific expertise and progress of a specific period of time the regulatory framework defines the minimal level that has to be documented before reaching the market. A further question is if this level should be the same for all types of drugs considering that if no authorized drugs are available for a clinical indication or in a subpopulation, how a physician can safeguard patient's right and health? Indeed, in an ideal world, all patients should be treated by drugs for which the maximum levels of efficacy, safety and quality have been granted after the evaluation of specific experimental data. Nevertheless, authorized medicinal products placed on the market do not cover all therapeutic needs; for instance, drugs for rare pathologies as well as suitable dosage forms or doses for paediatric population are not available. In the case of orphan medicines, the major obstacle to obtain market authorization is to prove their efficacy and safety since the conventional design used in clinical trials makes it difficult for this to be fully accomplished: there are too few patients, often geographically dispersed, and most of the time there is no other treatment available than the medicine under evaluation. This situation is even more complex when medicines are intended for the paediatric population, where ethical concerns have other implications [1-4]. Indeed, as many as half of all paediatric drug prescriptions were for either unlicensed medications or off-label use of licensed medications and 67% of paediatric patients received an unlicensed or off-label [5].

To meet the legitimate patients' right to receive treatment, the physician can prescribe pharmacological treatments other than for which the marketed authorization has been granted in the following scenarios: off-label prescriptions; compounded medicinal products; compassion use of medicinal products; prescription of medicinal products authorized in foreign countries [6].

The efficacy of all such therapeutic alternatives has not been proved according to the requirements established by the regulatory framework and the physician has to choose the active pharmaceutical ingredient on the basis of good sound scientific reasoning. The most suitable medicinal products will be selected while considering availability, costs and local regulatory requirements. If none of these alternatives are pursued, the physician shall initiate a clinical trial which assure safety to a high level and that protocols are carried out within ethical guidelines.

To avoid misuses of unlicensed drugs, the Authorities have to regulate their use. Probably a case-by-case approach is essential in order to establish the minimum requirements to fulfil. Indeed, in the case of the off-label use of drugs with market authorization, the quality is not under discussion, while the risk/benefit assessment is duty bound to physicians or regulatory framework. For example, in Italy at least a clinical study of Phase II as to be concluded.

The compassionate use normally is well regulated in all Countries. Extemporaneous preparations require attention to the quality other than risk/benefit aspects. Indeed, GMPs are not fully applicable in compounding pharmacies and adapted guidelines are elaborated (e.g. PIC [7]) or under discussion.

Considering these issues, can we pose limitations to the use of these products? Can we make a positive list? Probably not, above all is the light of the multiplicity of situations and the continuous progress of science.

The Public Administration must safeguard patients' right and health, evaluating the appropriateness of medical prescriptions. The physician is the one who has the knowledge and the tools to properly diagnose a pathology and, therefore, to select the most appropriate therapy. Obviously, to completely legitimate the patient's right to be treated it would be highly desirable to increase the number of granted marketing authorizations or to stimulate clinical studies. Even if the legislator defined a specific set of rules, there will be inevitably the need to fill the gaps with unlicensed drugs.

The more rigid the rules, the higher the risk of not legitimating the patient's right to be treated because a suitable medical product will not be available or cannot be prescribed.

The Public Administration should not limit a physician's freedom to prescribe only on-label approved drugs in an attempt to avoid misuse. The physician and the pharmacist have to be trained to assess the risk associated with all concerns to treatment or not a patient with an unlicensed drug. The Committee of Ministers of the Council of Europe enabled recently a resolution for extemporary preparations [8].

To favour the physicians' best practice and to support their choices, high-value information should be easily available. The Public Administration and agencies should develop a programme to ensure availability of data and public access to databases, after defining ad-hoc levels of safety and efficacy. To facilitate the work and to avoid duplication of studies, investigators and centres with specific expertise should be linked together in research networks. An effort should be made to include as many results as possible of clinical trials carried out in non-profit-making institutions.

On the basis of high-value evidence national and/or international scientific committees should also establish a decisional tree to support physicians' decision in prescribing drugs of any origins and to guide national health systems and health insurance schemes in the selection of reimbursable therapy or treatments.

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