

# Off-label drug use: the experience of the University Hospital of Catania from 2012 to 2015

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## Background

Off-label use is the practice of prescribing drugs for unapproved indications or age group, dose, or regimen of administration<sup>1</sup>. Off-label use is widespread worldwide and is more common in some populations, such as children, pregnant women and oncologic patients<sup>2-4</sup>. It is not uniformly regulated in different country. Despite the lack of a formal regulation in USA, it is legal for physicians to prescribe off-label drugs<sup>1</sup>.

In Italy, a comprehensive body of legislation has been produced in order to regulate off-label use. Law 648/1996 establishes that a medicine can be prescribed and reimbursed by National Health System (NHS) in the following cases: (1) drugs not yet available in Italy but recently approved in other countries; (2) medicines not yet authorized in Italy but currently used in clinical trials; (3) drug used for not approved indications. All these drugs must be included in a list by the Technical Scientific Commission (CTS) of the Italian Medicines Agency (AIFA). The inclusion of a drug on the list may be promoted by CTS, patient associations, hospitals, universities and scientific societies, based on new scientific evidences resulting from at least phase II clinical trials<sup>5</sup>.

Law nr. 94/1998 allows the physician, under his/her direct responsibility, to use an off-label drug based on new efficacy data. In this case, drug costs are not covered by NHS.

In compliance with national laws, Sicilian Department of Health has regulated the formal procedures that professionals must follow for off-label drug prescription. In an hospital setting, prescribers must request authorization for off-label treatment to the Health Director, and costs are covered by the hospital.

Regional Pharmacovigilance Centre of Catania, within the Clinical Pharmacology Program of A.O.U. Policlinico – Vittorio Emanuele, Catania, supports Health Director in the assessment, approval, management and follow-up of requests for off-label drug prescriptions according to L. 94/1998 and to L. 648/96.

The main objective of this project was to evaluate off-label drug use at the University Hospital of Catania.

## Methods

We used a database that collect all the requests for off-label use since Clinical Pharmacology Program has been activated in 2012. Off-label prescriptions were classified by field of application (oncology, rheumatology, cardiology, etc.) and divided according to L. 94/1998 and L. 648/96.

## Results

From 2012 to 2015, almost 990 requests for off-label use were evaluated for their appropriateness. Almost 57% of these requests has been approved according to L.94/1998 (Figure 1). As shown in figure 2, it's been detected an increase in the number of requests per year. Most of the prescription requests came from Hematology and bone marrow transplant division (28%) and Pediatric onco-hematology (19%; Figure 3). Figure 4 shows differences in the number of prescriptions according to L. 94/1998 and L. 648/96 per department. The top ten drugs per number of prescriptions are listed in table 1, differentiated according to L. 94/1998 or 648/96.

## Discussion

Appropriateness in off-label drug prescriptions must be carefully assessed in order to ensure this use occurs only in presence of data supporting a favorable risk/benefit profile.

The experience of Clinical Pharmacology Program of A.O.U. Policlinico – Vittorio Emanuele, Catania, shows that off-label use is frequent in special populations (oncologic patients, children), in accordance with literature<sup>2-4,6</sup>. The growing number of requests per year is probably due to the healthcare professionals awareness about procedures, considering that off-label use represent a common practice in clinical setting.

In future analysis we will evaluate the opportunity to submit requests of inclusion in the list of L. 648/96 of drugs used according to L. 94/1998, supported by important efficacy and safety data, in order to recognize their value and allow their reimbursement from NHS.