

## **Off-label drug use at the Policlinic-University Hospital of Catania, from 2012 to 2015: Focus on intra-ocular use of mitomycin**

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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. In Italy, a comprehensive body of legislation has been produced in order to regulate off-label use. L. 648/1996 establishes National Health System (NHS) can reimburse a drug (1) approved in other countries, or (2) currently used in clinical trials or (3) used for not approved indications. All these drugs must be included in a list based on new scientific evidences resulting from at least phase II clinical trials<sup>1</sup>. The inclusion of a drug on the list may be promoted by CTS, patient associations, hospitals, universities and scientific societies.

L. 94/1998 allows the physician to use an off-label drug based on new efficacy data, but in this case drug cost is not cover by NHS. In an hospital setting, prescribers must request authorization for off-label treatment to the Health Director, and costs are covered by the hospital.

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.

Clinical Pharmacology Program at the University Hospital of 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.

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.

Clinical Pharmacology Program of the Policlinic-University Hospital of Catania, within the Regional Pharmacovigilance Centre, 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.

### **Material and 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 have been approved according to L.94/1998, and

43% according to L. 648/96 (Fig. 1). Fig. 2 shows the number of prescriptions per department according to L. 94/1998 and L. 648/96.

We focused our attention over off-label prescriptions according to L.94/1998 and we found 54 requests applied for mitomycin (MMC) from Ophthalmology (Tab. 1). This drug is an antimetabolite used for decades in order to reduce postoperative scarring during glaucoma drainage surgery (trabeculectomy) through the inhibition of fibroblast activity. MMC can be applied intra-operatively on a sponge placed for one to five minutes between the conjunctiva and sclera at the start of the operation. Evidences supporting off-label use of MMC in glaucoma surgery were considered so strong that AIFA in 2016 granted reimbursement for this unauthorized indication according to L. 648/1996.

### **Conclusions**

The experience of Clinical Pharmacology Program of Policlinic-University Hospital of Catania, shows that monitoring off-label prescriptions in an hospital setting could allow to detect unmet medical needs and to identify drugs with favorable risk/benefit profile which could be included in the lists of L. 648/1996 and reimbursed by the NHS. 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 at the University Hospital of Catania, supported by important efficacy and safety data.

### **References**

1. [www.agenziafarmaco.gov.it](http://www.agenziafarmaco.gov.it)
2. Official Gazette n. 1000/2016