Agenzia Italiana del Farmaco

AIFA

Product Quality Office

Roma,

SUBJECT: Comments on EAHC Study on the availability of medicinal products for human use across the EU.

The present document has been drafted to provide comments on the "*Study on the availability of medicinal products for human use across the EU*" drafted by EAHC, based on the data collected and the experience accrued by the Product Quality Office in the management of medicines shortages since its establishment in 2009.

I. Summary of problem drivers

Table 1 displays three main drivers of availability problems:

a. Products not authorized.

b. Products not marketed.

c. Supply disruption and shortages, which include regulatory problems, manufacturing and supply chain disruptions and shortages determined by quotas/supply caps and parallel trade activities.

As a preliminary statement, though medicines pricing and reimbursements in Italy appear to be generally lower than in most EU countries, the Italian market does not seem to be considerably affected by authorization strategies nor by marketing issues. In fact, the Italian legislation established since 1997 the procedure to import, on a named patient basis, medicines that are not authorized in Italy and mandatory notifications and terms are provided by Legislative Decree no. 219/2006 (implementing EC Directive 2001/83) with respect to the starting date of marketing of a new authorized product, any interruptions and the regulatory consequences of a long-term suspension (the sunset clause). Anyhow, considerations may be made on the decision to waive the renewal of medicines taken by MAHs, when the costs of updating old dossiers

overweight the income of marketing gains when the renewal costs of the marketing authorizations cannot be recovered on the market.

With respect to the issues listed under the driver “Supply disruption and shortages”, we deem that, though the effect for the markets and the involved patients is the same — the issues reported represent distinct phenomena – regulatory procedures, manufacturing problems, distribution disruption, fixing of quotas, parallel trade – which all result in a remarkable reduction of product supplies on the market, but should not be distinguished between “actual” shortages and situations of unavailability of medicines.

Generally speaking, medicines shortages, excluding exceptional circumstances, can be handled and timely foreseen as MA Holders are supposed to provide, with at least two months prior notice, all relevant data on the causes, starting date of supply disruption and expected date of its restore (art. 34 of Italian Legislative decree 219/06 implementing art. 23a of Directive 2001/83/EC). Most initiatives and measures to reduce the shortage effects are agreed with the MAH of the product involved or with other MAHs of equivalent or analogue medicinal products. Furthermore, when the shortage is due to distribution disruptions, the MAH is required to guarantee a direct and timely supply, in compliance with the obligation of Article 81 of Directive 2001/83/EC.

On the other hand, situations of unavailability of medicines caused by massive parallel exports are not subject to any prior notice. In such cases, scarce information or cooperation may be provided by the MAH, who usually declares to have regularly fulfilled all supplying orders and, due to production forecasts and market shares, to be unable to supply the market with additional stocks of the product exported. Meanwhile, when the unavailability of medicines on the market is likely to be determined by considerable parallel exports carried out by wholesalers, attention must be focuses on the subjects operating in the distribution network.

Even different is the case of unavailability of medicines caused by quotas or supply caps imposed by the MAH (“contingentamento”), a business conduct which the Product Quality Office of AIFA has systematically opposed and contested as illegitimate, requiring the company, if necessary, to submit production and distribution data to verify the correct fulfilment of supply orders.

II. Parallel trade

With specific regard to paragraph 5.4 we would like to point out what follows:

a) the Public Service Obligation is in force also in Italy, as provided by article 1, paragraph 1, letter s) of Legislative Decree no. 219/2006. Nevertheless, the problems of unavailability of medicines increasingly determined in our country by parallel export activities implied a reflection on the need of new regulatory instruments for the management of market distortions, on condition that EU Treaty rules are met. An institutional cooperation between AIFA and the Ministry of Health led to the drafting of shared proposals to amend Legislative Decree no. 219/2006, finally adopted with Legislative Decree no. 17 of February 19, 2014, implementing EU Directive 2011/62. Consequently, the definition of PSO has been strengthened with the introduction of the following period: «*medicinal products for which specific measures have been adopted in order to prevent or limit situations of shortages or unavailability, even temporary, on the market or in lack of valid therapeutic alternatives, cannot be subtracted to the distribution and the sell on the national territory*».

b) Due to the low prices applied to most medicinal products, Italy is actually an exporting country. Besides, the number of wholesalers interested in parallel exports activities is growing and the related considerable effects on the availability of medicines on the market, since at least 2011, cannot be considered either "rare" or "occasional" any longer.

c) Finally, as above mentioned, when the unavailability of medicines is determined by an uncontrolled flow of products towards more remunerative foreign markets, such situations cannot be defined and handled as "*shortages*" but rather "*unavailability of medicines*". This distinction is relevant for two reasons:
   - the medicinal product is not in short supply at manufacturing level and is regularly placed on the market;
   - no cooperation may be provided nor obligation be imposed on the MAH who is generally unaware of wholesalers' export activities, even when their own medicinal products are concerned.

We hope our comments may be useful, in the view of a constant improvement and exchange of information and experience.

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