AGENZIA ITALIANA DEL FARMACO

Tutela Ricerca e Sviluppo per la Salute

Case C-606/17: feedback about questionnaire concerning public free supply of MPs in case of withdrawal

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Public Declaration of transparency/interests*

The view and opinions expressed are those of the individual presenter and should not be attributed to AIFA

Interests in pharmaceutical industry	NO	Current	From 0 to 3 previous years	Over 3 preavious years
DIRECT INTERESTS:				
1.1 Employment with a company: pharmaceutical company in an executive role	X	☐	☐	☐ mandatory
1.2 Employment with a company: in a lead role in the development of a medicinal product	X	☐	☐	☐ mandatory
1.3 Employment with a company: other activities	X	☐	☐	☐ optional
2. Consultancy for a company	X	☐	☐	☐ optional
3. Strategic advisory role for a company	X	☐	☐	☐ optional
4. Financial interests	X	☐	☐	☐ optional
5. Ownership of a patent	X	☐	☐	☐ optional
INDIRECT INTERESTS:				
6. Principal investigator	X	☐	☐	☐ optional
7. Investigator	X	☐	☐	☐ optional
8. Grant or other funding	X	☐	☐	☐ optional
9. Family members interests	X	☐	☐	☐ optional

*Carla Cantelmo, in accordance with the Conflict of Interest Regulations approved by AIFA Board of Directors (25.03.2015) and published on the Official Journal of 15.05.2015 according to EMA policy /626261/2014 on the handling of the conflicts of interest for scientific committee members and experts.

N.B. < I am not receiving any compensation>

Rationale

- The presentation concerns the result of the survey about the different MSs legal chances related to revoke/withdrawal of a MP according to the directive 2001/83/EC.

- For the purpose to guarantee the therapeutic continuity and the sufficient stock of MPs in order to cover the patient' needs and avoid shortages, MSs could explore different possibility – such as the "self –production" one - when the only MP authorized is withdrawn from the market.

Legal basis

- According to article 23a, par. 1, of directive 2001/83, "*if the product ceases to be placed on the market of a Member State, either temporarily or permanently, the marketing authorisation holder shall notify the competent authority of that Member State. Such notification shall, other than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product. The marketing authorisation holder shall inform the competent authority of the reasons for such action in accordance with article 123 (2)*".

Legal basis

- According to article 123 (2), "*the marketing authorisation holder shall be obliged to notify the Member States concerned forthwith of any action taken by the holder to suspend the marketing of a medicinal product, to withdraw a medicinal product from the market, to request the withdrawal of a marketing authorisation or not to apply for the renewal of a marketing authorisation, together with the reasons for such action*".

Case C-606/17

- The occasion for this reflection is a decision taken by the Italian Court of second instance (Consiglio di Stato), which asked the CJEU for a preliminary ruling about the interpretation of articles 1 and 2 of Directive 18/CE, setting out some principles about the public free supply of medicinal products, specifically radiopharmaceuticals.

- In the case in the subject, it exists only one MP authorized on the Italian market, and, for this reason, some authorized hospitals may prepare such kind of products on the basis of article 5 of directive 2001/83 in order to cover their specific needs.

Summary of the question

- The Consiglio di Stato set out some important principles about the public free supply of medicinal products, specifically radiopharmaceutical ones. In details, the Court rejected the appellant request of annulment of the decision of the Court of first instance concerning the infringement of article 6, par. 1, of directive 2001/83.

- According to the Court, this article does not prohibit to produce a radiopharmaceutical product for its free supply for the purpose of the public system self-production exclusively. This practice is admissible in case of absence of a marketing and manufacturing authorization.

Feedback questionnaire / the results

1. Have you ever experienced situations in which the MAH notified its intention to withdraw a MP, which was the only one available on the market at that moment?

- **YES** (IE, ES, BG, CH)

2. If yes, did you revoke the MA in such cases?

- **YES** (BG, ES, CH)
- **NO** (IE)

Feedback questionnaire / the results (2)

3. Did you provide for different solutions in order to balance the MAH rights and the public interest?

- **YES** (IE, ES)
- **NO** (BG, CH)

Feedback questionnaire / the results (3)

4. In the same case, after the withdrawal of the MP, did you provide for a system of self-production of the same MP?

- **NO** (IE, ES, BG, CH)

5. If not, have you implemented different system of hospital preparation in order to avoid the shortage?

- **YES** (IE, ES, BG)
- **NO** (CH)

The Irish experience (1)

- In general, in the Irish experience they do not revoke an authorisation which has been withdrawn, but, depending on the circumstances:

- If it is a proposed temporary withdrawal of supply, it could be that there is a regulatory issue and the solution is within our regulatory gift (e.g. a batch specific request).

- If it is a proposed permanent withdrawal of the MA, often it comes down to commercial matters (e.g. reimbursement price and other business decisions).

The Irish experience (2)

- From the Irish perspective, it could be better to facilitate the continued supply of a similar product that, although not authorised on the Irish market.

- In the absence of a MA and/or supply, if a hospital pharmacy was in a position to prepare a product under the exemptions in Article 3 of Directive 2001/83/EC that would be acceptable.

The Irish experience (3)

- HPRA may consider a batch-specific request application from a MAH in order to ensure the continued availability of a medicine on the Irish market. Such applications may be appropriate when product in full compliance with its registered MA dossier is temporarily unavailable or where action is proposed to bring a batch into compliance with the registered details. As part of any such request the MAH must provide assurance that the deviation from the registered MA is minor and non-critical and/or propose appropriate action to address the deficiency (e.g. repackaging with the approved product information). MAHs are strongly discouraged from applying for a BSR when a batch does not comply with the registered finished product specifications.

The Irish experience (4)

• However, in exceptional cases non-critical deviations may be considered on a case-by-case basis. Batch specific requests are limited in duration (normally no longer than three months) and can only be submitted for authorised medicines. MAHs are requested to read the HPRA Guide to Batch-specific Requests for Human Medicines and ensure that all points have been appropriately considered prior to submitting a batch-specific request using the dedicated application form.

The Spanish experience (1)

- The AEMPS maintains a face-to-face or teleconference meeting with the MAH in order to explore the possibility of continuing the supply if the withdrawal notification refers to a medicinal product that is considered essential for the national Health System, for any of the following reasons: absence of medications with the same composition or pharmaceutical form in the Spanish market and/or absence of effective therapeutic alternatives in the treatment of certain diseases. Its absence in the market can have an impact on the health system since the change of treatment of patients requires direct medical intervention (e.g. new prescription, etc.), in particular on off - label use.

The Spanish experience (2)

- Additional aspects, such as the market supply quota of medicines should also be taken into account when identifying these essential products, since there are medicines that could be considered essential only because they have a large percentage of the quota in certain markets.
- These meetings not always result in a solution, so the AEMPS may have no other alternative than revoking the MA. In such cases, the AEMPS tries to find a way to avoid the medicine shortage, such as: authorisation of an alternative medicinal product through a mutual recognition procedure with another EU country; import of a foreign medical product to cover the necessary treatments; recommendation of use on magistral formula for exceptional cases.

The Spanish experience (3)

- To date, a system of self-production of the same MP has not been provided in these situations. However, it is an option that could be raised in the future.

- However, in certain cases magistral formulation is used, but not only in hospitals.

The Bulgarian experience (1)

- With termination of the sales of the medicinal products from the Positive Medicines List and where within the frames of the relevant INN there is no other authorised medicinal products, the MAH shall notify in writing the Ministry of Health and the National Council of Medicinal Products Prices and Reimbursement not later than 18 months prior to the date of discontinuation of the sales.
- Prior to the discontinuation of the sales, the marketing authorisation holder is obliged to secure sufficient quantities of the respective medicinal product for satisfying the health needs.

The Bulgarian experience (2)

- According to the Bulgarian legislation, particularly Ordinance 10 of 17 November 2011, a medicinal product which is not authorized in Bulgaria may be prescribed by a commission of three physicians from a hospital under their direct personal responsibility. The commission have to write a medical statement by a protocol. Bulgarian Drug Agency coordinates the protocols. The Informed consent of the patient shall be attached to the protocol or the commission can make a decision to provide unauthorized MP to be available at the hospital for a particular patient. The medicinal products is supplied by wholesalers.

The Bulgarian experience (3)

- Where the treatment of a relevant sickness is without alternative in the country, for a concrete patient may be applied a medicinal products, which is authorised for use in an EU Member State, authorised for use under Medicinal Products in Human Medicine Act /MPHMA/, but is not marketed on the Bulgarian market. Annually, upon proposal of the hospitals after an opinion of the relevant national consultant on the profile of the sickness, the Minister of Health confirms a list of the medicinal products. The medicinal product shall be supplied upon a special order of a hospital according to Ordinance 10.

The Italian experience

- For the purpose to avoid the withdrawal and the related shortage of a MP, it has been subscribed a protocol of intent between AIFA, the Ministry of Health and the SCFM (Chemical and Pharmaceutical Military Site) which grants the possibility of a national production of some categories of products.
- In case of medicinal product, the MAH may release the license to the SCFM, who can produce and commercialize the MP autonomously.
- Another instrument based on the article 81 of Directive 2001/83 is the «public service obligation», which infringement is sanctioned in Italy by an administrative sanction, the suspension of the distribution authorisation and, as extrema ratio, by the revocation of the distribution authorisation.

The “self-production” system

- The “self-production” system may be regarded as an instrument of public innovation in the pharmaceutical field, otherwise as an alternative to patented essential innovative medicines.

- In that second scenario, it can be realized through a compulsory license by the NCA.

- The concession of the license limits the MAH power of exclusivity on the innovative MPs for the purpose to contain or limit their prices.

Final considerations

- The instrument of the compulsory license has not been achieved at a EU level, basing on the prevalence of the right of enterprise upon the right to health, interpreted as right to free access to the treatments.

- A proposal could be to recognize by law a larger power upon the NCAs for the purpose to prevent situation of abuse of the right of enterprise damaging the right to health.

Thank you for your attention!

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