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On 23 May 2015, the CPME Board adopted the "CPME position paper on rules regarding expiration dates of pharmaceuticals" (CPME 2014/074 Final)

CPME position paper on rules regarding expiration dates of pharmaceuticals

The Standing Committee of European Doctors (CPME)[1] represents national medical associations across Europe. We are committed to contributing the medical profession's point of view to EU and European policy-making through pro-active cooperation on a wide range of health and healthcare related issues.

Background

Every year a large amount of pharmaceuticals is destroyed. There are several reasons for that. One reason which is common for patients is that there are leftovers due to changed prescriptions or due to the fact that the treatment has been cancelled. Another reason for the destruction of pharmaceuticals, which is very common for the pharmacies, hospitals and the wholesale trade, is the fact that the expiration date has passed.

The expiration date of pharmaceuticals is usually set between 2 and 5 years. Expiration dates that are set for longer periods than 5 years are very uncommon. The delimitation of the expiration date is part of the approval procedure of pharmaceuticals and is based on the documentation of stability studies made by the producer. The producer needs to provide an expiration date and to specify how the pharmaceutical should be stored. There is currently no regulation on how long a pharmaceutical product should last; the standard of 2 to 5 years has been set rather through praxis.

In many countries military authorities have stockpiles of pharmaceuticals which are chemically and physically controlled every year. The results of these controls have shown that pharmaceuticals are very durable. An American study from 2012 analysed eight prescription-only medicines that were stored between 28 and 40 years in a pharmacy. 86 percent of the substances, contained at least 90 percent of the specified potency of the pharmaceutical.[2] 90 percent should be enough for the vast majority of the population since there is a difference between individuals when it comes to the absorption of pharmaceuticals.

Since a big proportion of pharmaceuticals has a high potency long after the expiration date, if they are stored and handled the right way, one might assume that pharmaceuticals are destroyed despite

[1] CPME is registered in the Transparency Register with the ID number 9276943405-41.

[2] Lee Cantrell et al. Stability of Active Ingredients in Long-Expired Prescription Medications. Archives of Internal Medicine 2012; DOI 10.1001/archinternmed.2012.4501.
http://archinte.jamanetwork.com/article.aspx?articleid=1377417

the high quality of the products. The waste of these pharmaceuticals has both an environmental and economic impact.

Current rules

There are two parallel procedures for the marketing authorisation of a pharmaceutical product within the European Union (EU). The pharmaceutical company may choose the centralised procedure which is handled by the European Medicines Agency (EMA) or the national authorisation procedure which is handled by the member states' national medical agencies. Within the second procedure, pharmaceutical companies have the option to go through decentralised or mutual recognition procedures: they can either apply for marketing authorisations in different EU member states (decentralised procedure), or they can apply, after having obtained a marketing authorisation in one member state, for this authorisation to be recognised in another member state (Mutual recognition procedure).[3]

Part of the approval procedure is composed of studies on the durability as well as on the longevity of the pharmaceutical. Rules regarding the needed documentation on longevity and durability are set in article 8.3.f) of Directive 2001/83/EC on the Community code relating to medicinal products for human use. Article 11.6.3) of Directive 2001/83/EC states that the summary of the product characteristics (smPC) should contain information regarding the expiration date, ie. its shelf-life. In addition to Directive 2001/83/EC, Guidelines from the European Commission, EMA and the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) define how stability studies should be conducted.[4]

Furthermore, the European Commission adopted guidelines for the cases when a producer wants to change the expiration date of a pharmaceutical product that has already been approved.[5] At the moment it is possible to shorten the expiration date without any detailed justification.

[3] For further regulatory information on marketing authorisation mechanisms in the EU, please click this link.

[4] - European Commission guideline on Summary of Product Characteristics (SmPC), among which shelf life:
http://ec.europa.eu/health/files/eudralex/vol-2/c/smpc_guideline_rev2_en.pdf
- EMA guidelines, specifically on stability testing:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000361.jsp
- ICH guideline on stability data:
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q1E/Step4/Q1E_Guideline.pdf
- EMA guideline on start of shelf-life of the finished dosage form:
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002917.pdf
- EMA guideline on Maximum Shelf-Life for Sterile Products for Human Use after first opening or following Reconstitution:
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003476.pdf

[5] European Commission guideline on the details of the various categories of variations to the terms of marketing authorizations for medicinal products for human use and veterinary medicinal products: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2010:017:0001:0044:EN:PDF

Waste and environmental impact

Pharmaceuticals are produced to be long lasting and durable. From an environmental perspective the long durability of a pharmaceutical product is a problem since it doesn't break down, instead it is accumulated in the nature and residues are found in the environment for huge periods of time.
Water contamination by pharmaceuticals is an environmental issue of great concern. Because of the high solubility of some pharmaceuticals, aquatic organisms are especially vulnerable to their effects. For those pharmaceuticals that need to be destroyed, due to a change in the prescription or other reasons, an effective take-back system needs to be put in place so that pharmaceuticals are utilised to their full extent, as it is of course crucial that pharmaceuticals benefit the patients and are not automatically destroyed because of short expiration dates.

In 2013, the European Commission has been asked to develop, in the framework of Directive 2013/39/EU on priority substances in the field of water policy, a strategy on water pollution by pharmaceutical compounds. The study issued on the matter addresses shelf life of medicinal products as one of the issues to be tackled.[6]

CPME recommendations

- CPME believes that short expiration dates of pharmaceuticals should be prohibited if not motivated by safety and efficacy.
- CPME calls upon the European Commission to consider the possibility of extending expiration dates for pharmaceuticals and thus revise the applicable rules. A crucial part of this revision process should be to analyse whether an extension of expiration dates would lead to a decrease in the destruction of pharmaceuticals. An extension of expiration dates could be envisaged at two levels: before the pharmaceutical is granted a marketing authorisation, ie. at the stage of the approval procedure; and after the marketing authorisation has been granted, ie. when the pharmaceutical product is already on the market. The second option would necessitate a reflection on how the Summary of Product Characteristics, SmPC, and the package leaflet could be updated.

[6] Study on the environmental risks of medicinal products – Final report – Executive Agency for Health and Consumers – 12 December 2013; see p. 169
http://ec.europa.eu/health/files/environment/study_environment.pdf