DECISION

No. 19/28.09.2007

on approval of Guideline on the application of certain provisions of Art. 729 and 730 of Law No. 95/2006 on Healthcare Reform, Title XVII – The medicinal product

The Scientific Council of the National Medicines Agency,
set up based on Minister of Public Health Order no. 485/09.05.2005, as amended, reunited on summons of the National Medicines Agency President in the ordinary meeting of 28.09.2007, in accord with Article 10 of Government Ordinance no. 125/1998 related to the set up, organisation and functioning of the National Medicines Agency, approved as amended through Law no. 594/2002, as further amended, agrees on the following

DECISION

Single article. – The Guideline on the application of certain provisions of Art. 729 and 730 of Law No. 95/2006 on healthcare reform, Title XVII – The medicinal product, according to the Annex which is integral part of this decision.

PRESIDENT
of the Scientific Council
of the National Medicines Agency

Acad. Prof. Dr. Victor Voicu

ANNEX

Guideline on the application of certain provisions of Art. 729 and 730 of Law No. 95/2006 on Healthcare Reform, Title XVII – The medicinal product

CHAPTER I
Introduction, legal basis, definitions

Art. 1. - This Guideline provides guidance concerning the manner of applying the provisions of Art. 729 and 730 of Law No. 95/2006 on healthcare reform, Title XVII – The medicinal product (further called „law").

Art. 2. – (1) Paragraphs (1) and (2) of Art. 729 of this law (which transpose the provisions of Art. 23a of Directive 2001/83/EC which implements a community code of the medicinal product), imply 2 specific obligations on behalf of the Marketing Authorisation Holders:

a) Following the granting of a marketing authorisation, the holder should inform the National Medicines Agency (further called NMA) concerning the effective date of the marketing of the medicinal product for human use in Romania, taking into consideration the various presentation forms authorised.

b) MAH should also notify the NMA of any temporary or permanent interruption of the medicinal product's marketing; such notification should be made at least 2 months prior to the cessation of the medicinal product's marketing, except for exceptional cases.

(2) The obligation mentioned in Art. 729 (3) of the Law concerning the volume of sales and the volume of prescriptions is not included in this Guideline.

Art. 3.- (1) According to Art. 730 (6) and (7) of the Law, any marketed authorisation which has not been followed by the effective marketing of the medicinal product in Romania, 3 years from being published, shall cease its availability; if an authorised medicinal product, previously marketed, does not show up in Romania for three consecutive years, the authorisation shall be invalidated.

(2) These provisions are known in the European Pharmaceutical Legislation patter as „sunset-clause".

For existing medicinal products, the 3-year period of non-marketing, which may lead to the marketing authorisation ceasing to be valid ('sunset clause') will start to be counted from 20 November 2005.

(3) According to Art. 730 (8) of the Law, the NMA may, in exceptional cases and taking into account the Public Health interests, allow abrogations from provisions of (6) and (7); such exceptions should be rigorously justified.

Art. 4 – (1) Provisions of Art. 729 have come into force 3 months from its publication.

(2) Starting from then, the Marketing Authorisation Holders were and still are obliged to inform the NMA concerning the date of the effective marketing and whether the medicinal product ceases to be marketed for all presentation forms of the authorised medicinal products.

Art. 5. – (1) Art. 730 of the Law has come into force [according to Art. 863 (d)], on the date of Romania's Accession to the European Union, meaning on 1 January 2007.

(2) Thus, for medicinal products which were granted a marketing authorisation prior to 1 January 2007 which own no marketed presentation form until this date, the three-year term which can lead to the cessation of availability of a marketing authorisation has started on 1 January 2007.

Art. 6. – The definitions below are based on the general principles issued in Chapter 1 of volume 2A of the *Notice to Applicants.*

a) (Actual) marketing: in accordance with Art. 729 (1) and (2) of the Law, a medicinal product is effectively marketed at the moment of „the placement within the distribution chain", meaning when it exits the marketing authorisation holder's direct control.

b) Marketing cessation: in accordance with Art. 729 (2) of the Law, the marketing cessation should be understood by anology with the marketing, as „cessation of the placement within the distribution chain", having as a consequence the depletion of the quantity placed the previous time within the distribution chain, shall no longer be available in order to be provided to Patients; the date of the marketing cessation is considered the date of the last placement within the distribution chain.

CHAPTER II

Requests for the notification of effective marketing and marketing cessation

Section II.1 Information to report to the NMA relating to the situation concerning the marketing of the medicinal product

Art. 7. – (1) According to Art. 729 (1) of the law, the holder should inform the NMA about the effective marketing date of the medicinal product for human use in Romania, taking into consideration the various authorised forms of presentation (meaning distinct information for each presentation form).

(2) The presentation form corresponds to a package size.

Art. 8. – (1) The Marketing Authorisation Holder should also inform the NMA if the medicinal product ceases to be marketed, either temporarily or permanently.

(2) When marketing cessation is the consequence of certain efficacy, safety and/or quality issues which already imply established procedure, reporting of this cessation does not interfere with the application of other relevant specific procedures (e.g. those relating to quality defects, pharmacovigilance issues etc.).

Art. 9. – (1) According to Art. 729 (1) of the Law, the marketing authorisation holder should inform the NMA about the effective marketing date, which shall be mentioned as day/month/year.

(2) By analogy, the marketing cessation should also be defined as an exact date.

(3) If the holder encounters difficulties in finding the exact date, the cessation date should however be defined as day/month/year, mentioning the last day of the closest week/month, in view of properly implementing the „sunset clause".

Section II.2. Reporting Calendar

Art. 10. - „Synthesis relating to the marketing situation" explains the image of the concerning the marketing authorisation of a certain medicinal product, at a specified point in the medicinal product's life-cycle, per presentation form, as follows:

Art. 11. – (1) Within 60 days as of the publication on the NMA website of this guideline, the marketing authorisation holders should submit a complete list of the situation concerning the marketing of all medicinal products authorised in Romania, using the form in Annex 1.

(2) The marketing authorisation holders should notify the NMA 30 days as of the marketing of a new medicinal product or a presentation form which hadn't been previously marketed.

Art. 12. – (1) Moreover, the NMA should be informed about any temporary or permanent cessation, of a medicinal product's marketing; cu ocazia unei asemenea notificări a încetării, the marketing authorisation holder further submits a complete updated table on the situation concerning the marketing of the medicinal product.

(2) Permanent or temporary cessations should be notified at least two months prior to the cessation, excepting certain exceptional circumstances.

(3)However, it is recommended that the NMA is informed as soon as possible, meaning as soon as the cessation is foreseen.

(4) If the marketing authorisation holder intends to cease marketing a certain medicinal product in a couple of months, yet has not defined an exact date, the holder may provide the NMA an interim date and then update it subsequently with more precise information.

(5) It is expected that the holder provides to the NMA detailed information on such a type of cessation; this information includes, for example, the reasons, duration of cessation, the intention of providing information to prescribers and patients to this extent etc.

Art. 13. – (1) It is possible that in certain exceptional circumstances the term of two months for the notification of the NMA concerning the marketing cessation of a medicinal product cannot be met.

(2) There may be certain situations in which the marketing authorisation holder cannot anticipate the interruption of the medicinal product's marketing within tyhe time frame established by the law, since the reasons for cessation are beyond his/her control.

(3) These situations shall be examined, case by case; they include major force cases [e.g. total arson of the manufacturing site, a natural disaster, major manufacturing difficulties, lack of the active substance or an ingredient of the medicinal product, including a packaging material, emergency-related concerns relating to safety or quality etc., as well as the cases described in Art. 819 (2) or Art. 828 and 829 of the Law].

(4) However, where the 2-month term cannot be met, the marketing authorisation holder shall inform the NMA as soon as the interruption is known or considered likely to occur.

Section II.3. Reporting format

Art. 14. – (1) According to the calendar described above, two copies on paper of the reporting form of the marketing of medicinal products, completed (accompanied by a covering letter), as well as the e-mailed electronic version of this reporting form shall be submitted to the NMA.

(2) The reporting form of the marketing of medicinal products is available in electronic format on the NMA website.

CHAPTER III
Public's access to information

Art. 15. – The NMA shall publicly announce the information concerning the marketing issue.

CHAPTER IV
Principles of the „sunset clause" monitorisation

Art. 16. – (1) The marketing authorisation remains valid if at least one presentation form is marketed and if at least one package size among the existent package sizes is marketed for that presentation form.

(2) In order to apply these rules, a marketing authorisation contains not only the initial authorisation, but all variations as well (e.g., additional presentation forms) and extensions (e.g., new doses or strenghts, new pharmaceutical forms), provided to the marketing authorisation holder under the same name.

Art. 17. – (1) According to Art. 730 (6) and (7) of the Law, a three-year period without marketing may lead to the application of the sunset clause.

(2) This will start counting from two different points as detailed hereafter.

Section IV.1. Marketing authorisation not followed by an effective marketing

Art. 18. – (1) According to Art. 730 (6) of the Law, any marketing authorisation which, in the first 3 years after having been issued, has not been followed by the effective marketing of the medicinal product in Romania, shall cease its availability.

(2) However, the start of the 3 years period will start running should coincide with the date when the medicinal product can be placed on the market by the marketing authorisation holder, meaning at the end of market exclusivity period of the reference medicinal product and at the end of other protection rules which must be respected, e.g. a patent.

Section IV.2. Previously marketed medicinal products, but which are no longer present on the market

Art. 19. – (1) According to Art. 730 (7), if a previously marketed medicinal product is no longer available for 3 years in a row in Romania, the authorisation shall cease its availability.

(2) The idiom „no longer available in Romania" shall be understood the same way as „ceases to be marketed" [Art. 729 (2)].

(3) Therefore, the term of the sunset clause will start running from the last date of the release into the distribution chain of the medicinal product.

CHAPTER V
Exemptions

Art. 20. – (1) According to Art. 730 (8) of the Law, the NMA may, under exceptional circumstances and taking into account the public health interest, provide exemptions to provisions under (6) and (7).

(2) Exemptions may be applied at any time of the marketing authorisation life cycle (i.e. at the time of the granting of the marketing authorisation, during the authorisation's life cycle, or approaching the expiry of the sunset clause period), depending on the exemption type.

Art. 21. – The marketing authorisation holder may be aware at the moment of the granting of the marketing authorisation that an exemption may be applicable, such as:

a) The medicinal products are about to be used in emergency situations, as an answer to certain threats to public health, recognised either by the WHO, or by the Community (Decision No. 2119/98/EC).

b) Antimicrobial medicinal products such as antibiotics, antivirals and immunological medicinal products (for active and passive immunisation), aimed at the prevention and/or treatment of diseases caused by bio-terror agents in response to an emergency public health need.

Art. 22. – (1) It is the duty of the marketing authorisation holder to explain the reason why such an abrogation should be applied, based due to public health aspects, under exceptional circumstances.

(2) Each justification should be notified to the NMA and will be considered on a case-by-case basis.

CHAPTER VI
Procedural aspects for the monitorisation of the sunset clause

Art. 23. - (1) Below is detailed the concept of the start and stop of the sunset clause period according to the main key-points of the marketing cycle of a medicinal product.

(2) The mechanism of the counting of the period could be revised by the NMA in the future, depending on the experience gained via events which may affect the determination of the start and stop of the sunset timer.

Section VI.1. Beginning of the sunset timer

Art. 24. – As previously mentioned, there are two situations which may lead to the start of the counting of the sunset clause period.

A. Granting of a marketing authorisation

Art. 25. – (1) At the time of the granting of a marketing authorisation, the medicinal product may not be immediately placed on the Community market.

(2) As a consequence, the term of the sunset clause starts running from the granting of the marketing authorisation or from the moment when the marketing authorisation holder may legally place the medicinal product on the market, considering the market exclusivity and other protection rules which have to be respected.

Art. 26. – (1) Information about marketing exclusivity of the reference medicinal product are available to the NMA, but the information relating to other protection rules are not known to the NMA.

(2) Therefore, MAHs are advised to inform the NMA about the of the expiry date of the other protection period to be respected as appropriate.

(3) This information should be notified within 60 days from the date of the granting of the marketing authorisation, otherwise the three-year period will start counting for a generic medicinal product after expiry of the 10 or 11 years of market exclusivity period of the reference medicinal product.

B. Temporary or permanent cessation of the medicinal product's marketing

Art. 27. - (1) In accordance with legal requirements, the marketing authorisation holder is responsible for informing the NMA about the marketing cessation.

(2) When there is no longer any presentation of the medicinal product actually placed on the Community market, the sunset timer will start running from the last date of release into the distribution chain of the medicinal product.

Section VI.2. Interruption of the sunset clause period

Art. 28. – (1) There are several situations which may lead to the interruption of the sunset clause period.

(2) Following the interruption, if the legal requirements are met, a new sunset clause timer may start running.

A. Initial Marketing

Art. 29. – The running of the timer of the sunset clause shall be interrupted at the moment of the first marketing of a presentation.

B. Re-marketing following a temporary marketing cessation

Art. 30. – As soon as a medicinal product is once more marketed following a temporary cessation, the sunset clause timer shall be interrupted.

C. According an abrogation

Art. 31. – As soon as an abrogation for a medicinal product is given, the sunset clause timer shall be interrupted.

CHAPTER VII
Reaching the sunset clause timer

Art. 32. - (1) It is the duty of the MAHs to monitor the sunset clause timer and to take appropriate measures, if they wish to maintain their authorisation.

(2) However, when reaching the moment of the sunset clause timer, the NMA shall inform the MAH about this.

ANNEX 1

Form concerning the reporting of the marketing issue of medicinal products (according to Art. 729 of Law No. 95/2006)

	Name of the medicinal product (invented)						
	INN			Additional information			
	MA Holder						

	Presentation forms			MA number	Authorised Yes/No	Actual marketing date	Marketing cessation date
No. crt.	**Dose/strength**	**Pharmaceutical form**	**Package size**				
1							
2							
3							
4							
5							
6							

…

EXAMPLE

Presentation forms			MA Number	Marketed Yes/No	Actual marketing date	Marketing cessation date
Dose/strength	**Pharmaceutical form**	**Package size**				
20 mg	tablet	15 tablets	001	Yes	01.01.2007	
50 mg	tablet	15 tablets	002	No		05.03.2007
100 IU/ml	solution for injection	1 vial	003	No		01.01.2007
100 IU/ml	powder and solvent for solution for injection	1 ampoule	004	Yes	DD/MM/YYYY	
200 IU/ml	solution for injection	1 vial	005	Yes	DD/MM/YYYY	

Instructions concerning the filling-in

A) Fill in this form if:
a) for all medicinal products authorised in Romania, in 60 as of the publication on the NMA webpage of the Guideline on the NMA notification concerning marketing and provisions relating to the sunset clause of the marketing authorisation's availability
b) 30 days as of the marketing of a new medicinal productand of a new presentatiom form
c) 2 months prior to the cessation of the marketing of any medicinal product's presentation form

B) Presentation forms (dose/strength, pharmaceutical form, package size) – one line for each presentation, in the order they appear in the MA, in the order of the authorisation. Placed on the market: specify „yes" or „no". Marketing/cessation date: specify in DD/MM/YYYY. Concerning the presentation forms placed on the market prior to 1 January 2007 please specify „01/01/2007" at the date of the placing on the market. Concerning the presentation forms which have not been placed on the market prior to 1 January 2007, please specify „01/01/2007" at the date of the marketing cessation.

C) If none of the presentation forms has been marketed following the granting of the MA, specify this in the box „additional information". For MAs granted after 01/01/2007, please specify the expiry date of „other protection rules", if needed. If, following a complete cessation, one or several presentation forms have been re-placed on the market, please specify this in the „additional information" box. If an exemption from the enforcement of the sunset clause has been granted, please specify this in „additional information".

D) Electronic sheets containing the fill-in instructions and the sample may be deleted. It is recommended to use several sheets within a single Excel document, yet ca single sheet shall be filled-in for each document.